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INNOCUOUS OILS USEFUL IN RHINOLOGIC PRACTICE, IN CONTRAST TO LIQUID PETROLATUM

FRANK J. NOVAK JR., M.D.
CHICAGO

It is of interest historically that the first use of mineral oil was for medicinal purposes. Samuel Martin Kier was the earliest refiner of oil. He first refined oil, not for lamps, but for medicine, a hundred years ago. When the oil springs of Pennsylvania were discovered, oil was skimmed off the water and the product used in a variety of "remedies." An editorial in the Chicago Daily News, which appeared on the one hundred and twenty-fifth Anniversary of Samuel Kier's birth, read as follows:

Kier's method of refining, the basis of most refining ever since, came naturally from the western Pennsylvania environment. Whisky was the great staple, not second even to pig iron in that region, and nearly every farmer had a still. Kier devised a special one-barrel still that derived something very much like modern kerosene from Pennsylvania crude, and after his medicine ventures had failed to meet expectations he turned to illuminating oil. Kier never attempted to patent his refining inventions. The American West in those days was full of his kind, men who were only secondarily interested in the money to be made out of "improvements."

The attention of people in general has been called to the possible deleterious results from uncontrolled self medication with nose drops. The intelligent public, which in these days is well informed about things medical, is keenly alert to the warnings that have been disseminated through the press and by radio regarding the indiscriminate use of oil in the nose. In view of the reaction to these warnings, it may be well to examine the evidence critically to see how much is really known about some of the medicaments used intranasally.

There is ample clinical and experimental evidence to show that the mineral oils are profoundly irritating to the alveoli of the lungs, both in the experimental animal and in the human being. Laughlen² in 1925 described the pathologic condition in the lungs resulting from the aspira-

Read at the meeting of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct 10, 1939

1 Footnote deleted

2 Laughlen, G. F. Pneumonia Following Naso-Pharyngeal Injection of Oil, *Am J Path* 1:407-414 (July) 1925

tion of oils Since then numerous writers have called attention to the fact that not only among infants but also among adults there is an increasing incidence of pulmonary disease due to aspiration of oil All of this is incontrovertible By extensive and conclusive experimental work Cannon and Walsh³ showed the following statements to be true

- 1 In the rabbit, when small doses of liquid petrolatum are instilled into the nose the oil finds its way almost immediately into the lung
- 2 This is followed promptly by an increased permeability of the alveolar wall and the exudation of albumin
- 3 With the lapse of time further extensive changes in the lung occur, which have been designated by various writers by such names as lipoid pneumonia and pulmonary paraffinoma Cannon and Walsh⁴ stated their purpose as follows

We wished to ascertain the early effects upon the lungs, particularly within the first few days, of medicated oils introduced into the nostrils of normal, "snuffles-free" rabbits The oil was given intranasally by means of a tuberculin syringe without a needle, in most instances in doses of 1 cc, 0.5 cc per nostril The rabbits were usually in a sitting position in a rabbit box, and under these circumstances the oil almost invariably gravitated to the anterior pulmonary lobes

The animals were killed in two or three days after instillation of the oil, the lungs fixed in situ with Zenker-formol solution, after which celloidin sections were prepared and stained with hematoxylin and eosin The following medications were used plain mineral oil, Vick's Vapo-Rub, mistol, pinoleum, benzedrine in oil, chlorotone inhalant and olodin The changes observed in the lungs were essentially similar for all preparations and were as follows Within twenty-four hours there was a focal edema of the involved portions of lung, extensive desquamation of septal cells, with many filled with large oil vacuoles The alveolar walls were thickened and in such areas there was definite focal atelectasis In some instances there was associated acute bronchitis, although usually this was absent The histologic picture was constant and showed definitely that such medicated oils and even plain mineral oil are toxic enough to pulmonary tissue to cause increased permeability of capillaries and leakage of albuminous fluid into the air spaces

In the light of this experimental proof of the extreme toxicity of liquid petrolatum to the pulmonary tissues and the clinical evidence of damage to the lungs from such oil, is there any justification for the use of oil in nasal therapy?

The inquiry resolves itself into consideration of three subjects (1) the therapeutic value of oil and the effects on the soft tissues of the nose, normal and diseased, (2) the evidence that oil finds its way into the lung of the human being as readily as into that of the rabbit, and (3) the relative irritant properties of the various oils, vegetable, animal and mineral

³ Cannon, P. R., and Walsh, T. E. Lipoid Pneumonia and Some Potential Dangers of Intranasal Medication, *Internat. Clin.* **3**: 109 (Sept.) 1938

⁴ Cannon, P. R., and Walsh, T. E. The Problem of Intranasal Medication, *Am. Otol., Rhin. & Laryng.* **47**: 597 (Sept.) 1938

Despite the admirable work of Lierle and Moore, Proetz, Hilding and others,⁵ it should not be assumed that the final and complete story of ciliary activity and other nasal function has been told. No one has as yet seen directly, through the microscope, the effect of oil, or for that matter of any other substance, on normal ciliated epithelium in its normal surroundings within the nose. The behavior of ciliated epithelium treated with various substances in tissue culture may be very different from the behavior of that epithelium in its normal habitat. The ciliated epithelium undergoes a multiplicity of chemical and histologic changes in its departures from the normal, and what the precise effects of various substances may be on these changes is totally unknown. Fox⁶ observed that intranasal spraying of rabbits with liquid petrolatum produced desquamation of surface epithelium when continued for nine months. It would be faulty reasoning to conclude that therefore spraying the same oil into the human nose for a few days has a deleterious effect on the surface epithelium.

Proetz, Lierle and Moore and Hilding studied the effect on ciliary action produced by oil alone and by oil as a vehicle for drugs. They observed the effect of oil on mucous streaming, and in general found that oil slows up or stops the movement of the mucous blanket. From these observations the following conclusion only is warranted, namely that in a normal nose with a normal mucous blanket oil interferes with the normal mobility of the mucous blanket. To conclude that oil is a deleterious agent is illogical. Oil as a therapeutic agent is not used in normal noses. What of the nose in which there is no fluid mucous blanket, or the one with perverted glandular (mucous) secretion or the one with abnormal ciliary activity? What experimental or clinical evidence is there that oil under these conditions is a deleterious therapeutic agent? In view of the fact that knowledge is so incomplete and fragmentary, a categorical statement that oil used in the nose is worthless, or even a deleterious therapeutic agent, is open to some question.

Cannon and Walsh⁴ reached the following conclusion:

In view of the fact that the maintenance of the physiological functioning of the nasal mucous membrane, and the promotion of adequate drainage from the nasal sinuses are the two essentials in the treatment of upper respiratory infections, weak saline solutions of ephedrine and neosynephrin appear to be the medications of choice for intranasal application.

This is a sound conclusion if more is not read into it than it says. Pathologic conditions sometimes occur in which there is no vestige of normal physiologic function in the mucous membrane, and as yet no experi-

5 Cited by Cannon and Walsh⁴

6 Fox, N. The Effect of Camphor, Eucalyptol and Menthol on the Nasal Mucosa, *Arch Otolaryng* **11** 48 (Jan) 1930

mental or other proof that oil is of no value, or that it is deleterious in its action in such cases, has been presented. The fact that it is gratefully received by the patient may not be without importance.

In general, one may say that there is not enough precise experimental evidence or enough valid clinical observation to justify any categorical conclusion regarding oil as a therapeutic agent in cases of nasal disease.

Now in view of what happens to a rabbit's lung when liquid petrolatum is dropped into the rabbit's nose, is there justification for the use of such oil in the human nose? It would appear that there is none. This point of view is further supported by the fact that there are wide differences of opinion among rhinologists regarding the actual therapeutic value of the use of oil in the nose.

However that may be, certain significant facts should not be lost sight of. Cannon and Walsh³ cited Ikeda, who found 106 cases of oil aspiration pneumonia reported by 24 authors in the ten years from 1925 to 1936. Among the laity the use of oil drops for the nose is one of the three most common types of self medication, the other two are use of cathartics and of acetylsalicylic acid. This implies consumption of large amounts of oil by an enormous number of persons, and yet over a ten year period there were only 106 reported cases of lipid pneumonia. Granting that many such conditions are undiagnosed, still the disparity between the number of reported cases and the huge number of persons who make a regular practice of using oil drops calls for some explanation. In all probability oil finds its way to the lung in the human being only when instilled into the nose under exceptional conditions. At this point it may be well to call attention to the fact that aspiration lipid pneumonia has occurred in adults who have taken liquid petrolatum by mouth for constipation. It is to be noted, however, that most of these patients took the oil in large amounts over long periods and moreover that some of them had dysphagia from one cause or another. These same people were in greater danger of lipid pneumonia from drinking cream or taking cod liver oil, for both of these substances are much more drastic irritants to the lung than is liquid petrolatum.

The animal oils, such as lard, cream and cod liver oil, have the greatest necrotizing action on lung tissue. The mineral oils rank next as irritants. The least irritating are the vegetable oils, such as cottonseed oil, sesame oil and olive oil. The relative toxicity of the three kinds of oils was determined by Pinkerton and Ikeda. The toxicity is dependent on the content of free acids, and the vegetable oils contain the least free fatty acids.

CONCLUSIONS

The use of any medicament in the nose, except ephedrine in physiologic solution of sodium chloride, is hazardous for some persons.

According to Ikeda, no type of oil should be used in the nose of persons with lesions of the tongue, lesions of the pharynx, or hemiplegia "or some other neurogenic disturbance" What applies to oil applies with equal force to practically all of the commonly employed drugs, whether in oily or in aqueous vehicles Furthermore, infants, debilitated children and the aged are more likely to aspirate fluids taken either into the nose or orally, and for these persons the use of liquid petrolatum or of any other kind of oil is clearly contraindicated But the use of oil when indicated, with care and judgment and in the rhinologist's office, may not be criticized, in view of the fact that legitimate differences of opinion exist regarding its therapeutic efficacy It is, however, safer to use vegetable oils than mineral oil The indiscriminate self medication with various oils by the laity should be condemned

30 North Michigan Avenue

BENIGN AND MALIGNANT TUMORS OF THE JAW

FRANK R SPENCER, M D

BOULDER, COLO

AND

CASPER F HEGNER, M D

AND

WILLIAM C BLACK, M D

DENVER

It has been favorably commented on at the recent meetings of the American Board of Otolaryngology that the younger otolaryngologists are examining the oral cavity with greater care than did the applicants of ten years ago who came before the board. While not all otolaryngologists are interested in or even qualified for oral surgery, all should thoroughly examine the mouth as a necessary part of any complete examination. The tongue depressor can be, and often is, used too soon to hold the tongue down and thus obscures pathologic lesions which should be examined and diagnosed early.

Many of the early lesions of malignant disease can be readily seen, but too many patients with such lesions put off having anything done until pain and external deformity compel them to seek relief. This is the experience of most physicians and surgeons on the staffs of state hospitals, so that the results following late diagnoses, operation and irradiation leave much to be desired, especially so far as cures are concerned. However, many patients have been made more comfortable and their lives prolonged. There are many factors which influence or even decide the prognosis and treatment of malignant neoplasms, as enumerated by McCarty,¹ such as the presence or absence of involvement of the lymph nodes, fixation of the growth, anatomic location, renal efficiency, the presence or absence of anemia, cardiac efficiency, size, age, duration and direction of the growth, loss of weight, lymphocytic infiltration, fibrosis, hyalinization and cellular differentiation. To these we should like to add previous operations and irradiation.

From the University of Colorado School of Medicine and Hospitals, Denver, Colorado

Read at the Sixty-Second Annual Congress of the American Laryngological Association, Rye, N Y, May 27, 1940

1 McCarty, W C Microscopic Grading of Tumors, Am J Roentgenol 37 365-367, 1937

GENERAL DATA

Age—In this series, the ages ranged from 2 weeks for the youngest patient to 81 years for the oldest. The average age in years was 49 plus. There were 4 patients of the ages of 2 weeks, 2 years, 8 years and 16 years respectively.

Sex—There were 3 female and 16 male patients in the series, which corresponds with the more frequent occurrence of malignant disease in males.

Occupation and Nationality—These were so varied as to be of no importance, especially in a small series.

Biopsy—In 11 cases a biopsy was performed to complete the diagnosis. In the 8 cases in which biopsy was not done, the patients did not come to operation.

Type of Tumor—In 13 cases a clinical diagnosis of carcinoma was made. In 4 of these the tumors were squamous cell carcinomas, and in 1 both squamous and basal cell lesions were present. We encountered 1 fibrosarcoma and 2 giant cell sarcomas, which, of course, are not true sarcomas, 1 malignant growth of undetermined type in a 2 year old child, 1 dentigerous cyst, and 1 sublingual cyst.

Metastasis—In 11 cases there was metastasis at least to the cervical lymph nodes.

Roentgen Therapy—In 10 cases roentgen therapy was given one or more times during the course of the disease.

Operation—Only 8 patients were operated on, as in many cases the tumor was inoperable.

Location—In 10 cases the tumor involved the right side of the lower jaw, in 7, the left side, in 1, the midline, and in 1, the upper jaw.

Follow-Up—The social service has been able to follow case 10. The patient is an Italian schoolboy who was 8 years old when he was observed by us, in December 1933 and January 1934. He had a fibrosarcoma of the right side of the lower jaw. His letter, dated March 7, 1940, says that he is feeling fine. Fourteen letters have been returned unclaimed. Five have not been answered and have not been returned.

REVIEW OF THE LITERATURE

Ivy,² in 1936, showed that adamantinomas, dentoperiosteal cysts, nasopalatine cysts, fibromas, fibroangiomas, benign giant cell tumors, carcinomas, ranulas, dentigerous cysts, etc., may all be of practical interest to the otolaryngologist. All of these and more may be seen and examined by the otolaryngologist first.

² Ivy, R. H. Tumors and Cysts of the Mouth and Jaws of Interest to the Otolaryngologist, *Tr. Am. Acad. Ophth.* 41:163-185, 1936.

New and Cabot³ have shown that by using the cautery, surgical diathermy, radium and the roentgen ray the operative mortality has been eliminated and recurrence greatly reduced. In reviewing the literature they mentioned the importance of Ohngren's work in the Holmgren service of the Sabbatsberg Clinic at Stockholm.

Patterson⁴ stated the belief that the diagnosis of benign and malignant lesions of the mouth or of the buccopharynx is a matter of no great difficulty. He stated that success or failure in treatment may depend to a large extent on whether the disease, when malignant, has invaded the cervical lymph nodes and that eradication of the disease in the neck is generally much more difficult than destruction of the primary tumor.

Padgett⁵ stated the belief that malignant cells in bone always go a greater distance in canaliculi of the bone than one would suspect. Excision of malignant tumors of the mandible must, therefore, be extensive if one expects to cure the patient.

Pond⁶ has reported a case of hemangioendothelioma of the upper jaw. We did not happen to have any hemangiomas in our series. However, this type of tumor is rather closely related to the giant cell tumors.

Sharnoff and Lisa⁷ have recently reported a case of adenocarcinoma of the mucous glands of the palate, with pulmonary metastases. We do not have a case of adenocarcinoma in our series. In 1 of our cases of basal cell carcinoma the tumor was not very prone to metastasis, but in our cases of squamous cell carcinoma metastasis was produced early. Adenocarcinoma and basal cell carcinoma are less likely to metastasize early.

Mead⁸ found sarcoma and carcinoma the most frequent malignant tumors of the jaw, the latter more frequent than the former. He stated the belief that the roentgen ray cannot differentiate early in the disease between benign and malignant tumors, especially periosteal sarcoma, but that the roentgen appearance of carcinoma of bone is fairly characteristic.

3 New, G. B., and Cabot, C. M. The Curability of Malignant Tumors of the Upper Jaw and Antrum, *Tr. Am. Laryng., Rhin. & Otol. Soc.* **41** 584-590, 1935.

4 Patterson, N. Treatment of Carcinoma of the Nose, Nasal Sinuses, Mouth and Buccopharynx, with Some Remarks on Diagnosis, *Tr. Am. Laryng., Rhin. & Otol. Soc.* **41** 1-34, 1935.

5 Padgett, E. C. *Surgical Diseases of the Mouth and Jaws*, Philadelphia, W. B. Saunders Company, 1938, p. 618.

6 Pond, C. W. Hemangioendothelioma of the Superior Maxilla with Case Report, *Tr. Pacific Coast Oto-Ophthalm. Soc.* **20** 78-82, 1935.

7 Sharnoff, J. G., and Lisa, J. R. Adenocarcinoma Arising from the Mucous Glands of the Palate with Pulmonary Metastases, *Arch. Otolaryng.* **31** 185-188 (Jan.) 1940.

8 Mead, S. V. *Diseases of the Mouth*, St. Louis, C. V. Mosby Company, 1928, pp. 550-551.

Mullin⁹ advocated surgical excision, surgical diathermy, radium and the roentgen ray for malignant growths in the mouth or the jaws. He cited Bloodgood's work at length. Mullin's percentages of fatalities show the necessity of early diagnosis and early excision.

Thomson¹⁰ found interference with movements of the jaw and involvement of the glands more frequent with carcinoma than with sarcoma in the early stages of the disease.

REPORT OF CASES

CASE 1—C J S, a white American boy aged 2 years and 4 months, was admitted to the hospital April 17, 1928, with a diagnosis of probable sarcoma of the left jaw. He died on July 1, 1928.

The patient was apparently perfectly well until July 1927, when the mother noticed a drooping of the left upper eyelid. This came on suddenly. She took the child to an oculist, who found the eyeball normal.

Three weeks before admission the mother noticed a swelling on the left side of the jaw, but she thought that this was mumps, because another child in the family had mumps. Three days after the swelling appeared the child fell and hit his forehead. A lump persisted at the site of the injury, but it did not cause pain or discomfort.

The dentist at the hospital extracted a tooth and with it some tissue for a biopsy. The tissue showed malignant disease.

The father was living and well at the age of 33. The mother was living and well at the age of 30. The mother had not had any miscarriages. The patient had one sister living and well at the age of 7 years.

The patient had had sore throat, and the left upper eyelid drooped. There was no history of abnormal development.

Physical examination revealed the child to be well developed. He was sitting up in bed, playing. The mental state was above the average for a child of his age.

The skull was symmetric. There were no exostoses. In the right temporal region there was an irregularity, firm and not tender. It was not movable in the skin. It was apparently proceeding from the skull.

The scalp was clean, and there were no visible scars. The hair was light colored. It was normal in amount and was soft and pliable.

The face was well nourished and fat. The left lower jaw was swollen and slightly tender. The mass was firm to the palpating finger and formed a spherical enlargement along the lower jaw. The left side of the forehead showed a slight scar.

The skin was pliable and was normal in color. It was warm. There was no excessive moisture. Over parts of the body, with no special predilection, there were small, irregular maculopapular patches, which had not been scratched by the patient. A small white scale could be removed from the top of each lesion. No abnormal pigmentation was seen.

9 Mullin, W. V. Treatment of Oropharyngeal Cancer, in Jackson, C., and Coates, G. M. The Nose, Throat and Ear and Their Diseases, Philadelphia, W. B. Saunders Company, 1929, pp. 329-330.

10 Thomson, St. C., and Negus, V. E. Diseases of the Nose and Throat, ed. 4, New York, D. Appleton-Century Company, Inc., 1937, p. 474.

The pupils were unequal The right was the larger The scleras were clear There was diplopia There was no nystagmus There was slight lagging of the lids, and the convergence was unequal There was no demonstrable disturbance of vision There were marked exophthalmos and restriction of motion of the right eye Upward motion was restricted The eyeball was pushed downward



Fig 1 (case 1)—Condition soon after admission

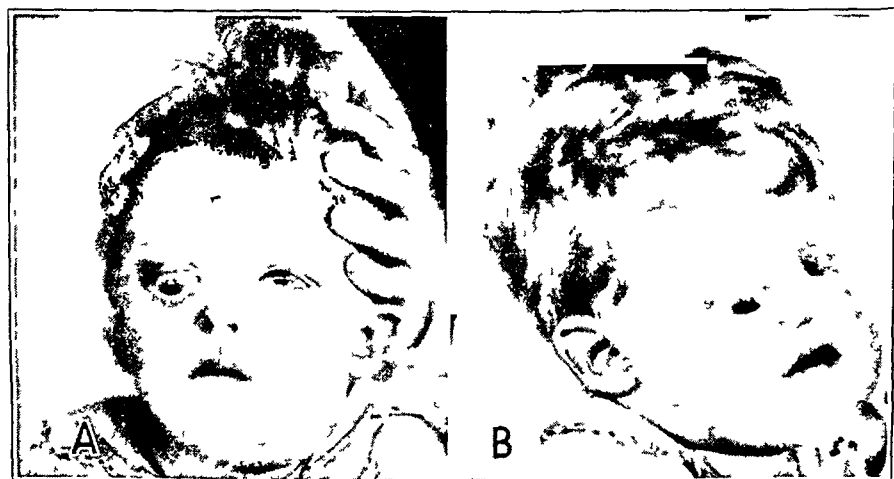


Fig 2 (case 1)—*A*, condition and appearance as the disease progressed *B*, appearance at a somewhat later stage

The ears were grossly normal There was no discharge and no tophi There were no deformities, obstructions or fissures of the nose

The teeth were in fairly good condition In the left lower jaw there was a healing socket where the tooth had been extracted There was no blood in the wound The gums about the socket were swollen and red The remainder of

the gums was pink and firm except on the left lower jaw, where a tooth had been extracted. There was no bleeding. The teeth were white, and there was no pegging. The breath was not offensive. There were no ulcerations except where the tooth had been extracted. There was no pigmentation. There was slight hyperactivity of the saliva but no drooling. The mucous membranes of the lips were pink. There was no herpes and no ulcerations or fissures.

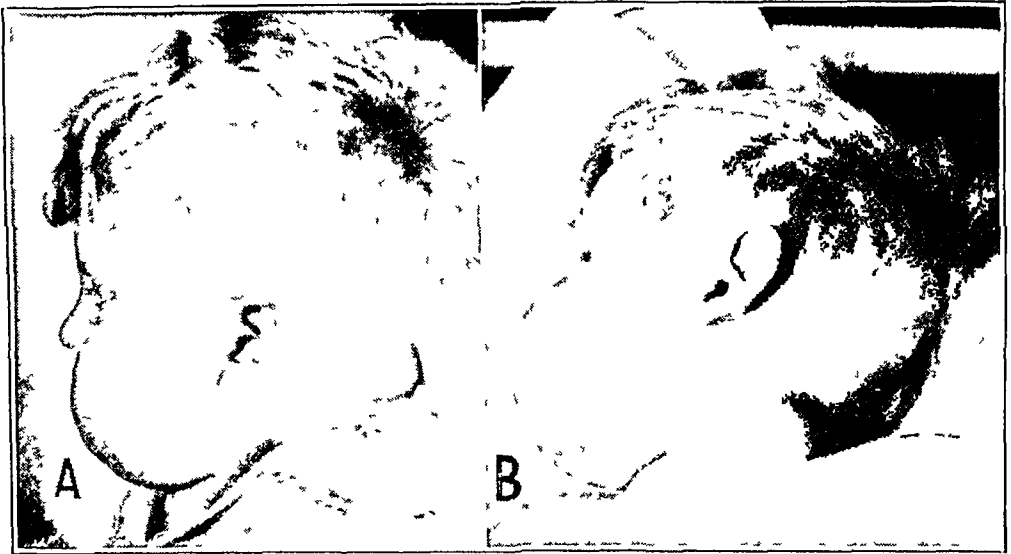


Fig 3 (case 1)—*A*, swelling about the lower jaw on the left. *B*, increased swelling about the lower jaw.



Fig 4 (case 1)—Loss of the right eye. The photograph shows the last stage of the disease, just before the fatal termination.

The tongue was not coated, and it protruded in the midline. There was no tremor. The tonsils were not enlarged, and there was no exudate. The pharynx was normal. The larynx was not examined.

The thyroid was not palpable. There were no thrills or bruits. Beneath the left sternocleidomastoid muscle there was a swelling, which was firm but not tender. This was apparently an enlarged lymph node. There was no stiffness of the neck.

The thorax was well developed and symmetric. There were no deformities. The respiratory movements were equal on the two sides. The respiratory rate was 28. There were no abnormal pulsations. The apical impulse of the heart was slight and was located inside the nipple line in the fifth interspace. There were no thrills or murmurs. The heart rate was 120. The vocal fremitus was not increased at the apices or over other parts of the lungs. The breath sounds were equal on the two sides. No rales were heard, and there were no friction rubs.

The abdomen was well developed. The shape was normal for a child of this age. There were pulsations. Peristalsis was not hyperactive. No tenderness and no masses were found. No rigidity, spasm or hernia was seen or palpated. The reflexes were normal. The edge of the liver was felt about 1.5 cm. below the costal margin and was smooth. The spleen was not palpable. The kidneys were not demonstrable, and the urinary bladder was not palpable. The child had been circumcised, and the testes were in the scrotum. The hermal rings were not palpable. Rectal examination was not made.

The lymph nodes were normal in the neck except on the left side, below the sternocleidomastoid muscle. Here there was a mass of enlarged lymph nodes. The lymph nodes were not palpable in the axillas, groins or epitrochlear regions. There was no rigidity or tenderness. There were no irregularities or deformities of the extremities. There were no abnormal or choreiform movements. There was no wasting, tremor or clubbing of the fingers. The nails were normal. The knee jerks were normal. The bicipital reflexes were normal. There was no swelling or stiffness of the joints.

The provisional diagnosis was malignant disease.

A biopsy was performed. The pathologist reported that the gross specimen consisted of a small portion of soft tissue adherent to an extracted tooth. Microscopic examination showed the tissue to consist of many small, irregularly rounded masses of fairly small round cells, the nuclei of which varied in size, shape and chromatin content and showed a few mitotic figures. These masses were separated by bands of fibrous tissue.

The pathologic diagnosis was malignant tumor of undetermined type.

The general surgical consultant considered intracranial involvement likely. He recommended neurologic consultation and observation. The ophthalmologist found the left eye normal, but the right disk was congested and the veins were tortuous on April 17.

The radiologist found the diaphragms smooth and the angles clear. The apex of the right lung was clear, but that of the left was dull. There was a mass in the apex of the left lung on April 17. The radiologist found no evidence of metastasis in the long bones on April 21. He found the right orbital plate indistinct, with evidence of bone destruction from malignant disease of the skull, on May 4. He also found that the dense area in the apex of the left lung, had increased. On May 12 there was no radiologic evidence of metastasis in the spine or in the pelvis. However, on May 21 the mass in the apex of the left lung was larger than on previous examinations.

Nothing of importance was revealed in eight urinalyses performed between April 17 and June 28.

The erythrocyte count was 5,070,000 and the leukocyte count 6,000 per cubic millimeter, 82 per cent polymorphonuclears and 18 per cent small lymphocytes, on April 17. The value for hemoglobin was 82 per cent by the Dare test. On May 1 the value for hemoglobin was 55 per cent by the Dare test. The erythrocyte count was 4,150,000 and the leukocyte count 12,800 per cubic millimeter, with polymorphonuclears 77 per cent and small lymphocytes 23 per cent.

There was moderate achromia. On June 4 the value for hemoglobin was 43 per cent by the Dare test, the erythrocytes numbered 2,750,000 and the leukocytes 11,600 per cubic millimeter, with polymorphonuclears 69 per cent and small lymphocytes 31 per cent. There was moderate achromia. The Wassermann reaction of the blood was negative on April 25.

When the patient was admitted to the hospital, on April 17, the mass attached to the left jaw was about the size of a walnut. The mass over the right orbit was the size of a marble. Both were firmly attached to the bone beneath.

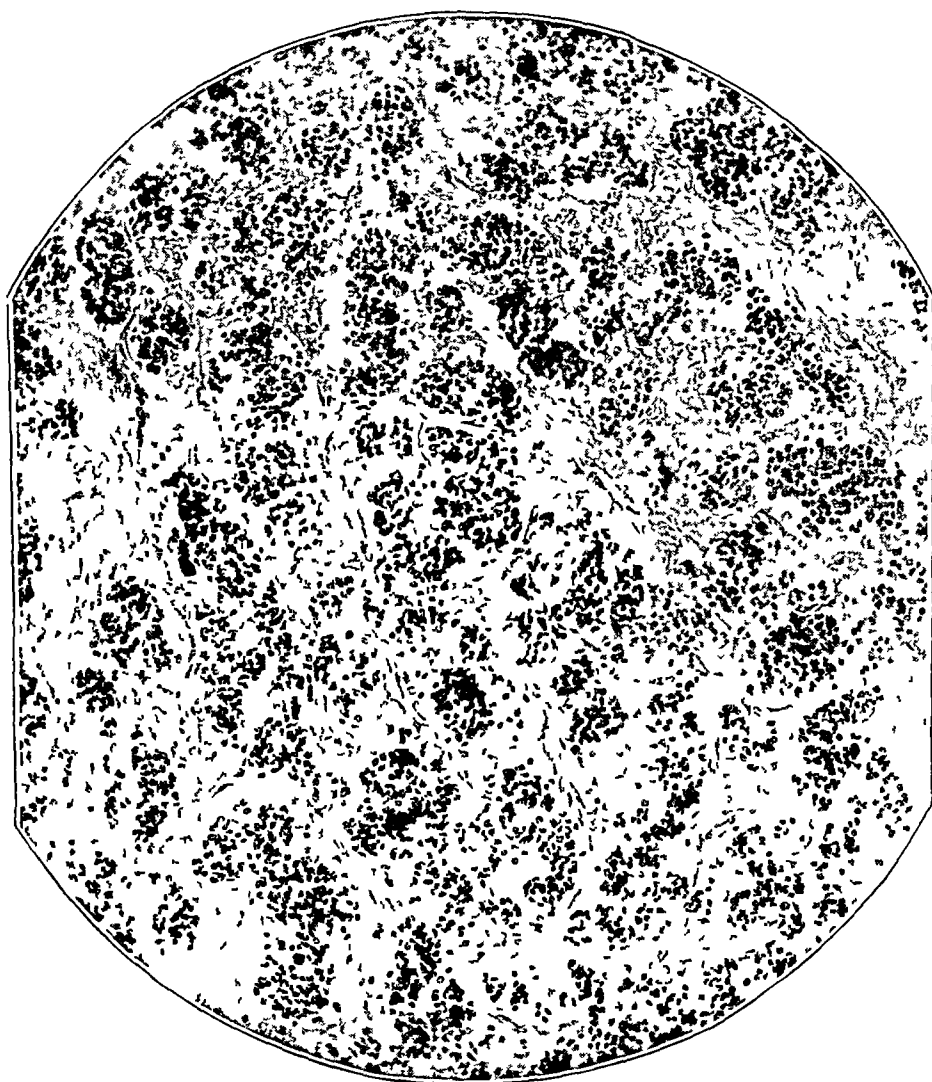


Fig 5 (case 1)—Photomicrograph of a malignant tumor of an undetermined type.

On April 24, high voltage roentgen therapy was started. The general condition was good. On April 28 the child was irritable and drowsy. He wanted to be let alone. The tumors were increasing in size.

On April 30, Coley's fluid (a mixture of erysipelas and *Bacillus prodigiosus* toxins) (M 1/30) was given, but there was no reaction. On May 1, M 1/15 was given, with a moderate reaction, and the temperature rose to 102 F for two days. The child was irritable and drowsy. His condition was not good. Coley's fluid was subsequently given as follows, without reaction: May 8, M 1/6, May 10, M 1/4, May 12, M 1/2, May 15, I, May 18, II.

The temperature was 101 F on May 20. Administration of Coley's fluid was discontinued.

The masses slowly increased in size, so that codeine sulfate ($\frac{1}{4}$ grain [0.015 Gm] *pro re nata*) became necessary to relieve pain.

By June 15 there was bleeding from the mouth, and the exophthalmos was so marked that there was necrosis of the eye. The dose of codeine sulfate had to be increased to $\frac{1}{2}$ grain (0.03 Gm) *pro re nata*. By June 18 the eye was sloughing, and the child was in great pain. His progress rapidly became unsatisfactory, and death occurred on July 1.

CASE 2—W. T. D., an American man aged 73, a painter, was admitted to the hospital on Feb. 28, 1927, and discharged unimproved on March 16. The diagnosis on admission was carcinoma of the left jaw.

His chief complaint was of a painful lump on the left side of the lower jaw.

All of his teeth had been extracted twenty-five to thirty years before admission. Two or three years later he noticed a roughening in the left cheek, which gradually became larger, but he had not had any pain until six weeks before admission. At the time of admission the lump was about the size of a small egg and seemed to be increasing rapidly in size. He stated that it had increased in size rapidly during the two weeks before admission. The pain was getting worse at night. A smear taken in the outpatient department showed Vincent's angina.

The patient's father had died at the age of 70 from pneumonia. His mother had died from intestinal obstruction at 60. He had three brothers living and well. One brother had died in boyhood from an unknown cause. Another had died as the result of an accident. A third had died from measles. Two sisters had died from influenza. A third had died in infancy. There was no family history of cancer, tuberculosis, heart trouble, nephritis, diabetes or nervous disease.

Physical examination revealed the patient to be well developed but undernourished. He was not acutely ill. There was a tumor on the left side of the face and neck, at the angle of the jaw. The left axillary lymph nodes were enlarged. The spine was normal. The knee jerks and plantar reflexes were normal. The pupils reacted to light and in accommodation. There was a bilateral pterygium. The ears were normal. The nasal septum was deflected. The mouth was edentulous. The tongue, tonsils and uvula were normal. There was a large tumor in the left cheek, which was fissured. The neck contained a hard, smooth, tender tumor at the angle of the jaw, about $1\frac{1}{2}$ inches (3.2 cm) wide, extending from the external auditory meatus down to the middle of the left side of the neck.

The movements of the chest were fairly good, and the chest moved en masse. The expansion of the lungs was fairly good. The tactile fremitus was unchanged. There was dullness in the upper thirds of both lungs anteriorly and posteriorly. There were rales in the upper thirds of both lungs posteriorly, with an increased whispered voice on the right posteriorly. The heart was not enlarged. The point of maximum impulse could not be seen or felt. The sounds were of fair quality, with a slight systolic murmur at the apex. The pulse was regular and of normal rate. The blood pressure was 135 systolic and 75 diastolic. The abdomen and the genitourinary organs were normal. Rectal examination was not made. The extremities were normal.

The provisional diagnosis was malignant tumor of the lower jaw.

On March 2 a biopsy specimen was taken with the region under local anesthesia (1 per cent procaine hydrochloride). A piece of tissue was removed from the inside of each cheek. There was a cauliflower-like growth on the lower jaw in the back part of the mouth on the left side, which was beginning to proliferate.

This looked like a carcinoma. A piece 1 inch (2.5 cm) long on the right side of the lower jaw anteriorly looked like a cauliflower mass and was probably carcinoma.

The pathologist reported that the section from the right cheek consisted of a papillary tumor. There was marked downgrowth of the rete pegs into the underlying tissues. These became branched and anastomosed in some areas. The tumor cells were of the basal cell variety and showed variations in size, shape and

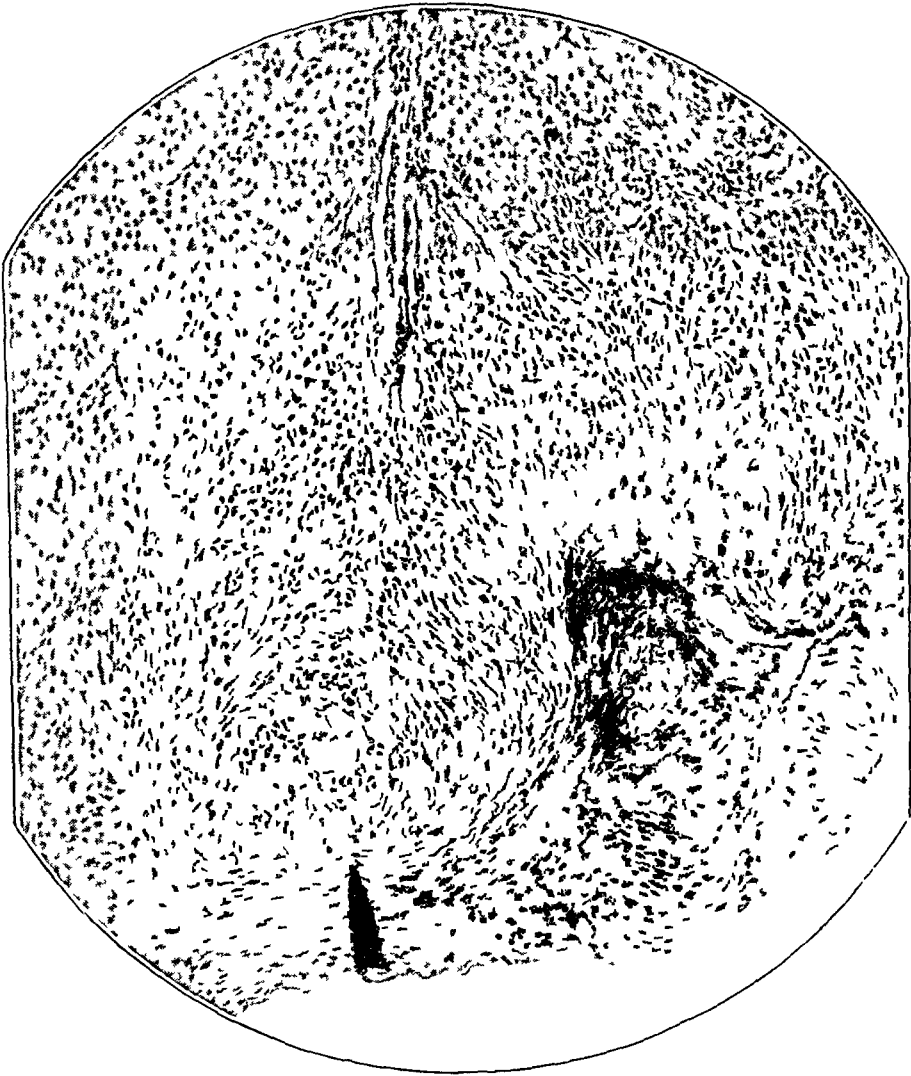


Fig. 6 (case 2)—Photomicrograph of a squamous cell carcinoma of the left cheek.

staining qualities. Many mitotic figures were seen. There was marked round cell infiltration around the downgrowing epithelium, mainly of the mononuclear variety. In one area there was a nest of tumor cells which appeared more like the squamous cell than the basal cell variety.

The pathologic diagnosis was basal cell carcinoma of the right cheek.

The pathologist also reported that the surface epithelium from the left cheek showed marked proliferation and downgrowth into the underlying tissues. In one small area the cells were of the basal cell variety, but in the remainder of the section they were of the squamous cell type. There was marked variation in size,

shape and staining qualities of the cells noted. Many mitotic figures were seen. There was no tendency to pearl formation. There were some infiltration by mononuclear cells and some necrosis.

The pathologic diagnosis was squamous cell carcinoma of the left cheek.

Three urinalyses, on March 1, 2 and 3, revealed practically no abnormality except that on March 3 some fatty degeneration was evident. On March 2 the value for hemoglobin was 85 per cent by the Dare method. The erythrocytes



Fig 7 (case 2)—Photomicrograph of a basal cell carcinoma of the right cheek.

numbered 4,820,000 and the leukocytes 7,150 per cubic millimeter, with polymorphonuclears 73 per cent, small lymphocytes 26 per cent and eosinophils 1 per cent.

A consultation by the surgeon, the dermatologist and the radiologist was held. They decided that the tumor was inoperable, and the roentgen ray was used for treatment as a palliative measure. The patient was discharged unimproved after the first roentgen treatment on March 16.

CASE 3—A. H. C., an American man aged 81, retired, was admitted to the hospital March 28, 1929, with a diagnosis of fibrosarcoma of the left jaw. He was discharged improved on April 10.

His chief complaint was of a growth under the left side of his jaw for the previous four months. He believed that the growth had increased in size for some time before admission. He began to have pain ten days before admission. The pain was sharp and severe at times and was present constantly as an ache extending up to the left temple. There was marked tenderness to pressure.

His mother had died from tuberculosis, and his father had died from a stroke. One sister and two brothers had died from unknown causes. He had four brothers living and well. There was no history of cancer, Bright's disease or cardiac or nervous disease in the family.

He had had the usual childhood diseases. He had had a fever fifty years previously. He had had a stroke at the age of 69. He had had a tumor removed from his right ear eight years previously and another from his left ear a year previously. He also had had a tumor removed from under the tip of his tongue a year previously. All were pronounced cancers by his physicians. He had used coffee and tobacco moderately, but he had not used alcohol.

He had taken cold easily. He bundled up excessively. Recently he had had dyspnea on exertion. His feet and hands got cold easily. His appetite was good. He had no distress after meals. His bowel movements were fairly regular. He had nocturia (three times) each night. He had some dysuria and tenesmus. There was no history of gonorrhea or syphilis.

Physical examination revealed him to be well nourished, ambulatory and apparently in acute distress. The skin was dry and scaly. There was patchy pigmentation of the face. The head and the scalp were normal. There was bilateral arcus senilis. The pupillary reactions and the ocular movements were normal. The ears, nose and throat were normal.

The mouth was edentulous. The tongue and gums were normal. A mass the size of a hazelnut was present on the inside of the lower jaw, just to the left of the midline. It was hard, round, smooth and not freely movable. This seemed to be a continuation of a larger mass, which was apparent and palpable below and anterior to the jaw. This was also hard but was irregular in shape and apparently firmly adherent to the mandible. It was tender to palpation. There was one anterior cervical lymph node on the left, the size of a bean. This was moderately hard but not tender. The thyroid was not palpable.

The thorax was symmetric, and there was good expansion. There was definite paravertebral dullness from the third to the seventh dorsal vertebra. The heart was of normal size. The tones were of good quality and rhythm. The rate was 80. The blood pressure was 165 systolic and 75 diastolic.

The abdomen was soft, and there was no tenderness. No organs or masses were palpable. The genitalia were normal. The prostate was of normal size and consistency. It was not tender, and there were no mucosal irregularities. The extremities were normal. The abdominal reflexes were active, but the patellar reflexes were sluggish. The achilles reflexes were also sluggish.

The provisional diagnosis was sarcoma (?) or fibroma(?). The possibility of a carcinoma with recurrence in the submaxillary gland on the left with involvement of the mandible was considered.

Urinalysis on March 28 and April 2 and 9 gave practically negative results.

On March 28, the value for hemoglobin was 80 per cent by the Sahli test. The erythrocytes numbered 4,200,000 and the leukocytes 6,000 per cubic millimeter, with polymorphonuclears 79 per cent, endothelial cells 19 per cent and basophils 2 per cent. The Wassermann reaction of the blood was negative.

The general surgical consultant on March 30 stated the belief that the tumor was malignant and advised removal if roentgen examination justified this.

The radiologist reported that roentgenograms of the chest were normal. There were no osseous changes in the films of the jaw. He considered the patient suitable for operation.

On April 2, with the region under local anesthesia produced by H. M. C. no. 1 (a mixture said to contain hyoscine, morphine and cactine) and 15 cc of 0.5 per cent procaine hydrochloride, the tumor was removed from the jaw. An incision was made by the surgeon over the apex of the tumor below the ramus of the jaw.

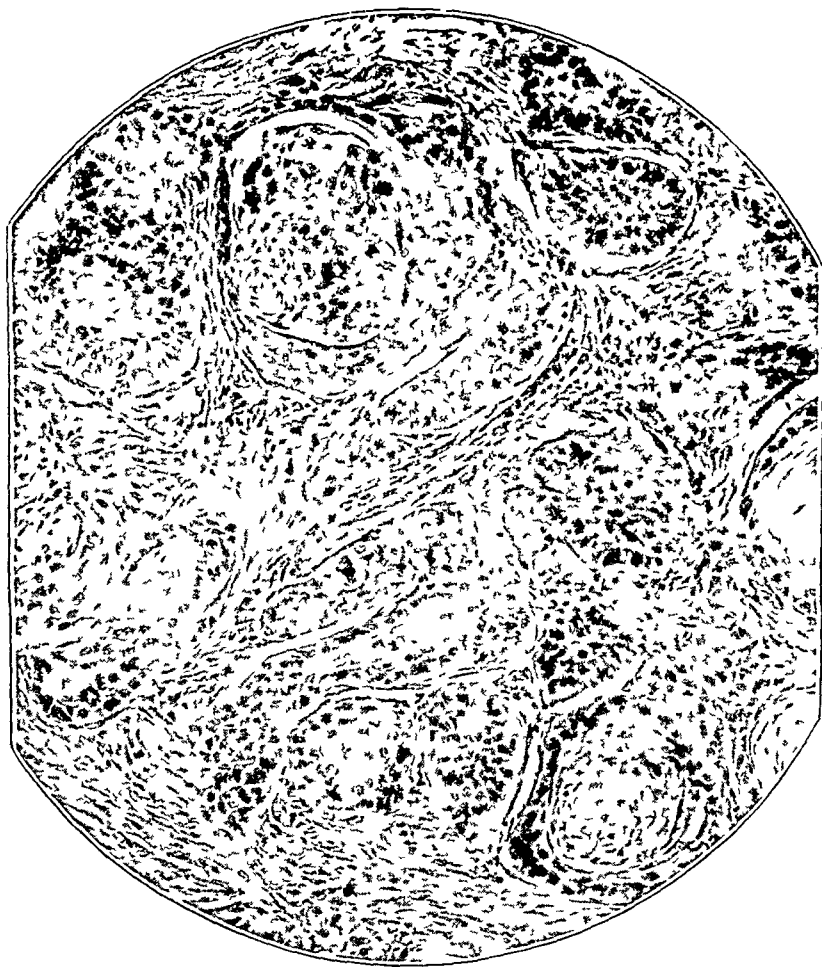


Fig. 8 (case 3)—Photomicrograph of a squamous cell carcinoma of the lower jaw.

The tumor was exposed inferior to the muscle involving the anterior belly of the digastric muscle and the salivary gland. In separating some of the adhesions about the tumor it was ruptured, and a great deal of creamy, thick granular material was discharged. A wide dissection was done below and included part of the digastric muscle with the submaxillary gland. Part of the periosteum of the jaw was also removed, and the bone was curetted. The bare bone was swabbed with Harrington solution. The wound was lightly packed with iodoform gauze and the platysma sutured with plain catgut. The entire wound was closed with interrupted silkworm gut.

The pathologist reported that the specimens consisted of three small pieces of pale, soft tissue removed from beneath the jaw. The largest was 2.5 cm in length. Microscopic examination showed the largest piece of tissue to be made up of large, irregular masses of squamous epithelial cells, the sizes and shapes varying greatly. The nuclei showed numerous mitotic figures and varied in size, shape and chromatin content. In many places the cells formed round masses of hyalinized and keratinized concentrically arranged cells, forming "pearl bodies." Sections of a lymph node showed that it included two small areas of squamous epithelial cells similar to those described.

The pathologic diagnosis was squamous cell carcinoma of the lower jaw.

On April 10 the wound had completely healed, and the patient was discharged on leave.

He was readmitted on June 19. He said that an abscess had formed at the corner of his mouth the day after he was discharged. His family physician opened this and evacuated a large amount of pus. This abscess had drained constantly since. He had lost about 10 pounds (4.5 Kg) since his discharge. He had had almost constant pain and at times it had been unbearable. His face had been badly swollen at times. During the week before readmission his left eye had been swollen shut. He had not been able to wear his lower plate.

Examination showed swelling and induration of the buccal surface of the left cheek. There were several masses the size of a bean under the tongue on the right side. These were solid. The cutaneous surface of the left cheek was as hard as stone. The swelling extended from the zygoma to the clavicle.

Urinalysis on June 20 revealed no abnormality. The value for hemoglobin was 85 per cent by the Dare method. The erythrocytes numbered 5,010,000 and the leukocytes 12,300 per cubic millimeter, with 83 per cent polymorphonuclears, 11 per cent small lymphocytes and 6 per cent eosinophils. The Wassermann reaction of the blood was negative.

On June 22, high voltage roentgen therapy was started and continued for some time through the outpatient department. He was discharged from the hospital on June 23.

He was readmitted on July 27 and died on August 15. He failed gradually after his third admission, in spite of high voltage roentgen therapy. He required a sedative each night to enable him to sleep. He was mentally confused and refused food. He was comatose from August 12 until he died. Permission for autopsy was refused.

CASE 4—I M., a white man aged 58, a farmer, was admitted to the hospital on April 24, 1929, and first discharged on August 20 as unimproved. The diagnosis on admission was malignant disease of the jaw.

His chief complaint was of pain in his back. This was worse in the right interscapular space. He had numbness of the extremities, with weakness and staggering when he walked.

Two years before admission to the hospital he had been thrown from a wagon in a runaway and had fallen flat on his back. For some time after this he had had pain in the interscapular region. This had lasted only a short time but had returned after overworking during the threshing season, six months before admission. The pain had been dull and bearing down when he had been up and about. It had been relieved when he was flat on his back.

He had been able to do his work until he had an attack of influenza, three months before admission. During this period of three months he had been able to do very little work. For two or three weeks before admission he had spent

most of his time in bed, and he had been weak. He had been unable to control his legs, staggering when he tried to walk. For a week or more before entering the hospital he had at frequent intervals experienced a numbness and tingling which affected the upper parts of the arms and the entire lower extremities either simultaneously or separately. This was most marked in the right lower extremities. It lasted only a few moments at a time. It was relieved by rubbing. His best weight was 120 pounds (54.4 Kg), twenty years ago. His weight was 120 pounds six months before admission. At the time of admission it was 109 pounds (49.4 Kg).

He thought that his father was dead. His mother had died at the age of 30 from an abscess in her throat. He did not know about his brothers and sisters.

He had had chills and fever each summer until he was 12 years of age. This had been called malaria. He had lived in Iowa. He had had the usual childhood diseases except scarlet fever and diphtheria. He had had influenza in 1918 and 1919. He had been in bed two weeks but had made a complete recovery.

His wife had had a cough and hemorrhages since an attack of influenza in 1918. She had given birth to one child, she had not had any miscarriages.

He had had chronic nasal catarrh for years, with some nasal obstruction. He stated that he usually had a severe cold each fall, which often "hung on" all winter. He had had pleurisy when 12 years old but not since. His appetite had been poor for two weeks before admission. It had been good before that. He had had gas and flatulence, and his urine had been muddy for two weeks before admission. It had had a foul odor and had been reddish for three months. He did not have dysuria or straining.

General physical examination showed him to be small, with a masklike expression, the face appearing lopsided because of the prominence of the left side of the lower jaw. He held his head forward and was reluctant to turn it to either side because it produced pain in the interscapular region. There was a soft, fluctuant mass about 1 inch (2.5 cm) in diameter over the bregma. The hair was gray.

The pupils reacted to light and in accommodation. There was no strabismus, ptosis or lid lag. The ocular movements were normal. The nose was externally normal, and the ears were normal.

There was a smooth, elastic tumor attached to the lateral and inferior surfaces of the lower jaw on the left side. This extended from the jaw posteriorly about 2 inches (5 cm) forward. This tumor within the mouth filled the depression between the cheek and the gum. It was covered by mucous membrane in which there were many dilated capillaries. The patient said that this tumor had begun to grow after a tooth was extracted, a year before. During the preceding three months it had grown more rapidly. The mouth was edentulous. The tongue was slightly coated. It protruded with a slight tremor and somewhat to the right. The uvula deviated to the left. The gag reflex was active, and there was no weakness of the palate. The tonsils were submerged, and the pillars were injected. There was slight cervical adenopathy.

The chest appeared flat and sunken. The shoulders were rounded. The right scapula was somewhat more prominent than the left. There was moderate tenderness in the interscapular space and over the trapezius muscle at the base of the neck on the right. There was slight respiratory excursion. The resonance was slightly impaired, and the breath sounds were diminished over the right side of the chest posteriorly and laterally.

Dulness of the heart percussion was 1 inch (2.5 cm) outside the nipple line on the left and 1 cm to the right of the right sternal margin. The point of maximum impulse was fairly palpable in the fifth interspace, $\frac{3}{4}$ inch (1.9 cm) outside the nipple line. The sounds at the apex were of good quality. There was a faint, short systolic murmur, not transmitted. There were no thrills. The aortic second sound was greater than the pulmonic. The peripheral vessels felt stiff. The blood pressure was 145 systolic and 110 diastolic.

The abdominal viscera were normal. There were no masses or tenderness and no muscle spasms. The abdominal reflexes were present. The cremasteric reflexes were not elicited. There were palpable lymph nodes in both inguinal regions.

Pain sense was diminished throughout the lower extremities except over the malleoli. Touch and temperature sense seemed unimpaired. The patellar jerks seemed exaggerated. The achilles jerks were present. The plantar reflexes were normal. There was no ankle clonus. The gait was ataxic. The patient watched the floor. He walked on a wide base, and he lifted his feet rather high. He staggered, especially to the right. The Romberg sign was somewhat suggestive.

The provisional diagnoses were (1) chronic nephritis, (2) adhesive pericarditis, (3) sarcoma of the lower jaw with metastases to the lungs, (4) multiple sclerosis, and (5) old injury of the right shoulder.

The neurologic consultant found moderately well marked and apparently rapidly progressive involvement of the cervical and upper thoracic portions of the spinal cord (diffuse) secondary to osseous and probably carcinomatous pathologic change in the spine. He believed that the prognosis was poor and recommended treatment for the primary disease.

The radiologist found the stomach orthotonic. There was no incision or filling defect. There was active peristalsis. The duodenal cap was of medium size and was normal. There was a trace of barium sulfate in the stomach at the end of six hours, with the head of the meal in the hepatic flexure. After twenty-four hours some barium was evacuated. After forty-eight hours part of the appendix was visualized, a trace of barium remaining in the colon. The gastrointestinal tract was normal. The dorsal and lumbar portions of the spine were normal. No diseased vertebrae were made out in the cervical portion of the spine. There was marked kyphosis in this region. However, the films were not entirely satisfactory.

Gastric analysis and examination of the feces gave negative results. Examination of the spinal fluid, including the Wassermann test, gave negative results. Chemical study revealed the blood and the spinal fluid to be normal. Nineteen urinalyses during four months showed reactions for albumin ranging from 1 plus to 4 plus. There were many granular and hyaline casts, with some pus cells. After one month's treatment the casts disappeared and the pus cells diminished. The value for hemoglobin ranged from 100 to 86 per cent by the Dare method. The erythrocytes numbered 5,320,000 and the leukocytes 9,600 per cubic millimeter. The polymorphonuclears ranged from 68 to 81 per cent. The small lymphocytes ranged from 26 to 19 per cent. The Wassermann reaction of the blood was negative.

Roentgenograms taken in the outpatient clinic before the patient was admitted to the hospital showed metastatic nodules in the chest.

On May 2 the patient showed paralysis of the right lower extremity. He failed rather rapidly. On May 4 the left side was apparently becoming involved. The evidence seemed to point toward involvement of the cord. By May 10 the paralysis had progressed, extending to the region of the fifth and seventh dorsal vertebrae.

He had involuntary movements of the bowels and of the urinary bladder. By May 18 he had a bed sore on the left hip. The pain was so severe that he had to be given narcotics frequently. He received supportive treatment while in the hospital. The multiple metastases to the lungs, ribs, spine and legs made surgical intervention impossible. He was discharged unimproved on August 20.

The diagnosis at the time of his discharge was general carcinomatosis.

CASE 5—J W S, a white man aged 73, retired, was admitted to the hospital on Sept 2, 1929, and discharged September 13. The diagnosis on admission was tumor of the left side of the lower jaw.

His chief complaint was of a lump on the left side of the lower jaw, which was tender. He also complained of stomach trouble.

His illness began in November 1928, with stomach trouble. He felt weak and had some fever. He had nausea and vomiting. He had not felt well since, but he had tried to work. He was hungry most of the time, but whatever he ate made him sick and caused a great deal of pain. There was no particular food which bothered him. He had lost 40 pounds (18.1 Kg). He had not vomited blood or coffee grounds, and he had not passed any blood or tarry stools. He had had an ulcer of the anus in March 1929. He urinated frequently.

In the early part of July a lump had appeared on the left side of the lower jaw, which was tender. This was painful at the time he was admitted to the hospital. It interfered with opening the mouth.

His father had died of senility at 75 and his mother at 86. He had three brothers living and well and three sisters living and well. One brother had died at 67 of apoplexy. One sister had died at 25 of puerperal sepsis.

He had been married at the age of 40 but separated from his wife two years later. His wife had not had any miscarriages or abortions. He had had diphtheria at 25 and pneumonia at 30. He stated that he had had no childhood diseases. He had had gonorrhea at 48. He stated that he had never had syphilis.

He had been cross eyed from birth. His right eye was the weaker. His right ear had been quite deaf since an abscess had ruptured at the age of 56. His nose was obstructed, and he often had a sore throat. He was short of breath, and his feet swelled if he was on them very much. He had some palpitation.

General physical examination showed him to be poorly nourished. He was lying quietly in bed and was in some distress. He was only fairly cooperative. His hair was sparse and gray. There was marked internal strabismus. The right eye had poor vision. There was an arcus senilis. The eyes reacted to light but only poorly in accommodation. The ears were grossly normal. There was occlusion of the external nares, which was more marked on the left. There was a firm red mass of tissue, which was not painful. The teeth were all out. The tongue was clean and protruded in the midline. The tonsils were small and submerged. On the left side of the lower jaw, extending from about the region of the mental foramen to the ramus, was a firm, tender mass which seemed to be attached to the bone. This was not movable and did not extend into the mouth.

The thyroid gland was barely palpable. There was no tracheal tug. There were no palpable lymph nodes in the right cervical chain. In the left anterior cervical chain there were a few palpable lymph nodes inside the jaw.

On the right side of the chest posteriorly, from the vertebral body of the scapula to the vertebral spines, was an area of diminished resonance. There was another, located anteriorly from about the second to the fourth rib, and this extended about 5 cm to the left of the sternal margin. In both of these areas

there was diminished to absent breathing, but no rales were heard. The heart sounds were of poor quality and faint. There were no murmurs. The pulmonic first sound was greater than the aortic second sound.

In the abdomen there was marked spasm of the rectus muscle on the left on even very light palpation. Some muscle spasm was noticed also on the right. On deep palpation no tenderness was elicited. In the midline, about 3 finger-breadths above the umbilicus, there was a small, firm palpable mass.

There were no fissures of the rectum. There were some hemorrhoids. The prostate was nodular and firm. The external genitalia were normal. The extremities and reflexes were normal.

The provisional diagnosis was carcinoma of the jaw, lung, stomach and prostate.

On September 3 the radiologist reported that the stomach was normal, except for ptosis and that the duodenum showed no ulcer. There was some periduodenitis of the second portion, presumably due to pressure by the ligament of Treitz or the colic artery leading to the hepatic flexure. The colon showed stasis, with marked ptosis of the hepatic flexure. However, the radiologist found an area of pulmonary infiltration of the upper lobe of the left lung, presumably due to metastatic carcinoma.

The laboratory reported the urine to be normal on September 2 and 10. The value for hemoglobin was 88 per cent by the Dare test on September 5, the erythrocytes numbered 4,460,000 and the leukocytes 4,650 per cubic millimeter, with polymorphonuclears 67 per cent and small lymphocytes 33 per cent.

The urologist, who saw the patient on September 11, found no carcinoma of the prostate and no spinal complaints.

The radiologist found rarefaction of bone at the site of the tumors. The primary site of the carcinoma was not found but was believed to be in the stomach. The condition was considered inoperable, and he was discharged with his condition unchanged.

He was readmitted on December 24. His jaw, stomach and prostate were all more painful than on discharge. His mental condition made him very refractory. This was probably secondary to the more or less constant use of opiates. He was discharged to the Colorado Psychopathic Hospital.

CASE 6—F B, a white single American man aged 52, a farmer, was first admitted to the hospital on May 1, 1930, with a diagnosis of carcinoma of the lip.

His chief complaint was of swelling of the lip and neck. He had been cut on the lower lip at about the age of 31. This was at the left corner of the mouth, and the cut was deep. It was not sutured. Ever since the accident he had noticed a small nodule in the lower lip, at about the center. He had cut this nodule often while shaving. In June 1929 he had noticed a small, superficial white lesion near the center and front of the lower lip. It retained its diameter of about $\frac{1}{4}$ inch (0.64 cm) until August of the same year, when he had been in an automobile accident. He had been badly cut in the lower lip by automobile glass. After this the mass had grown larger and had assumed a cauliflower appearance. It had grown in toward the lower gum. The lower teeth had been knocked out at the time of the accident.

He had had a number of treatments with radium. The seeds had been implanted in the lower lip, but the apparent relief or cure had been followed soon by reappearance of the growth. The nodules in the neck had even increased in size. The lymph nodes in the neck had been enlarged for at least one and

one-half months before admission. He had had a course of high voltage roentgen therapy in the Colorado General Hospital, through the outpatient department, just before he was admitted to the hospital.

His health had always been good. He had had the usual childhood diseases. He had had influenza in 1918 and pneumonia in 1900. He stated that he had never had gonorrhea or syphilis. His hip had been broken in 1917. He had not had any operations.

His father had died at 92 from old age. His mother had died at 40 from an unknown cause. He had one brother living and well at the age of 54. He had one sister living and well at 63. One brother had died from an accident. Two sisters had died. There was no history of familial diseases.

He had often had tonsillitis. He had had pleurisy in 1908, but no cough and no hemoptosis or dyspnea.



Fig 9 (case 6)—Photograph of a patient with an epithelioma of the lower lip and involvement of the lower jaw. This was taken after the operation.

Physical examination showed him to be well developed and well nourished, he was lying quietly in bed, in no evident pain or discomfort. He was alert and cooperative.

His skin was of the normal texture, with some roughness and lack of pigmentation about the angles of the mouth. There were roughness and redness of the skin on each side of the neck and face. The hair was of normal texture and distribution. The head was normal in size and shape. There were no exostoses, and the sinuses were not tender. The pupils reacted to light and in accommodation. The ocular movements were normal. The ears and nose were normal. The breath was foul, and the tongue was coated. The tonsils were fairly large. The pharynx was injected.

In the lower lip there was a cauliflower-shaped mass about the size of an egg, and this was indurated. It was tender and irregular in outline. It was ulcerated from the mucocutaneous junction to the base of the gums. There was a large area of induration. The glands along the mandible were very large. The submental and the superior and anterior cervical lymph nodes were very large.

The lungs were clear. The heart was not enlarged. The sounds were of good quality. The first sound at the apex was muffled. The rate was normal, and there were no murmurs.

The abdomen was flat and relaxed. There were no masses or tenderness. There was no hernia, but both inguinal rings were slightly enlarged. The genitalia were normal. The extremities and reflexes were normal.

The provisional diagnosis was epithelioma of the lip.

The laboratory reported five urinalyses as giving practically negative results from May 1 to 20. On May 1 the value for hemoglobin was 80 per cent by the Dare test. The erythrocytes ranged from 4,800,000 to 5,250,000 per cubic millimeter at two examinations, and the leukocytes from 4,900 to 6,000, with the polymorphonuclears 67 to 84 per cent, small lymphocytes 14.5 to 33 per cent and eosinophils 1.5 per cent. The Wassermann reaction of the blood was negative.

The radiologist found no bony involvement of the mandible. The sockets of the recently extracted teeth were visible. He advised extraction of the remaining teeth.

On May 2, with the patient under ethyl chloride and ether anesthesia, induced with great difficulty, five sixths of a parallelogram-shaped carcinoma of the lower lip was removed. A large inflamed gland on the right side of the inferior maxilla was removed. This was probably the submaxillary gland. No other glands were felt. The typical Grant incision was made for restoring the lip, barring mucous membrane from the inner side of the jaw and denuding the fascia and the masseter muscle on each side in order to secure approximation.

The pathologist reported that the section of the lip measured 5 by 2.5 by 2 cm. There was an ulcerated area in the center of the resected tissue, which measured 2 by 1 cm. Adjoining this there was a large, firm, nodular swelling beneath the skin. The tissue cut with resistance, and the cut surface was white.

The lymph node measured 2.5 by 2 by 1 cm and was firm. The cut section showed several irregularly round white areas.

Microscopic examination of tissue from the lip showed an area of ulceration and necrosis on the surface, surrounded by stratified epithelium. Strands of epithelium extended down into the corium in many places. The corium showed extensive infiltration with sheets of epithelial cells. In some places these cells occurred in broad columns which branched and anastomosed, while in other places they were arranged concentrically, with keratinized cells toward the center. In a few areas the concentrically arranged cells showed extraordinary enlargement and deformity in many regions, and the nuclei varied markedly in size, shape and chromatin content. Many of the cells were multinucleated, and many mitotic figures were seen. The cytoplasm of the cells was pale staining and vacuolated. The stroma supporting these cells was infiltrated with lymphocytes, plasma cells and some polymorphonuclear leukocytes.

The lymph node showed only a few scattered areas of lymphoid tissue. Practically the entire gland had been replaced by masses of epithelial cells, which had the same appearance as had those described for the lip. In several places there were groups of necrotic cells, some of which were extensive.

The pathologist's diagnosis was squamous cell carcinoma of the lip with metastatic carcinoma of the cervical lymph nodes.

The patient's convalescence was rather uneventful. On May 8 there was some infection at the left angle of the mouth and of the sutures in the midline. However, he continued to improve. The redness, swelling, tenderness and discharge gradually diminished. By May 19 there was very little drainage but much swelling. On May 24 the roentgenograms revealed no infection of the jaw.

He was discharged on May 27 and told to return to the outpatient department for high voltage roentgen therapy on June 9.

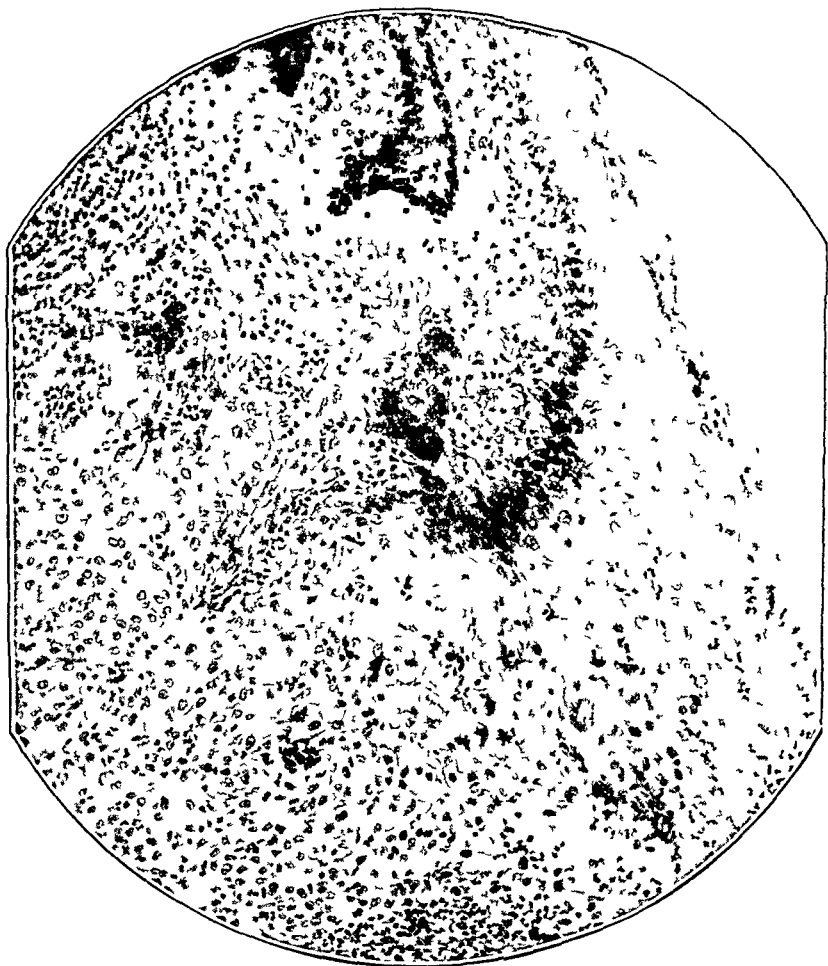


Fig 10 (case 6)—Photomicrograph of an epithelioma of the lower lip

An abscess of the lower lip developed a few days after he was discharged. This was at the site of the former incision. He was readmitted for this. It was opened, and hot irrigations were ordered. He was discharged the following day.

On August 25 he was readmitted to the hospital on account of a stony hard mass intimately connected with the mandible. This was tender but was not discharging into the mouth. At the extreme lower border of this mass the mandible appeared roughened. On the right cheek, just over a point midway between the angle and the symphysis, was a mass about 4 to 6 cm in diameter, which was ulcerated and was discharging very foul pus. This mass was fixed to the bone beneath. It was tender and painful. There was a brownish induration along the

right side of the neck This extended down almost to the clavicle and up to the tip of the mastoid This area felt hot and was tender

The diagnosis was carcinoma of the right cheek, with metastases and osteomyelitis of the right mandible

The laboratory reported eight urinalyses as giving practically negative results between August 25 and September 23

On August 28, with the patient under sodium amytal, nitrogen monoxide and oxygen anesthesia, the recurrent carcinomas were excised from the cheek down to the mandible, and the tumor in the neck was cauterized

The pathologist reported that the specimen of skin and subcutaneous tissue from the face measured 4.5 by 3.5 by 3.5 cm One surface was covered by skin, in the center of which was a foul-smelling ulcer 2.5 by 1.5 cm The skin around the ulcer was raised, smooth and pale The subcutaneous tissue was firm The cut surfaces showed a central red and necrotic area surrounded by dead, white, firm tissue A smaller piece consisted of a narrow strip of skin and soft attached tissue which looked like lymphoid tissue The microscopic sections corresponded with those previously examined for this patient, except that a greater amount of mucous gland was present

The pathologic diagnosis was squamous cell carcinoma of the lip with metastatic carcinoma of the cervical lymph nodes

During October and the first week of November the patient received extensive radium therapy in the hospital The roentgen ray showed some destruction of the mandible on the right

CASE 7—E H, a white man aged 55, a farmer, was admitted to the hospital Aug 5, 1932, with a provisional diagnosis of malignant disease of the jaw

His chief complaint was of a painful ulcerated area on the right side of the lower gum for two months

His father was living and well at 76 His mother had died at 73 of a cerebral accident He was one of five children One had died in infancy of an unknown cause Four were living, and all were well except the patient His maternal grandmother had died of cancer of an unknown location There was no history of tuberculosis, diabetes, renal disease, heart disease, hay fever, asthma or insanity in the family

The patient slept well for eight hours each night He ate his meals at regular hours He drank coffee twice a day, but no tea Until two months before admission he had smoked 4 ounces (113 Gm) of tobacco each week Just before admission he had chewed 1 pound (0.5 Kg) of tobacco each week He had not used alcohol or drugs

He had been married at the age of 32 His wife had been pregnant eight times She had had two early miscarriages Six children were living and well His wife had died at the age of 41 from intestinal obstruction His greatest weight had been 194 pounds (88 Kg) His average weight was 170 pounds (77.1 Kg) His weight on admission was 160 pounds (72.6 Kg) His height was 5 feet 11 inches (180.3 cm)

His general health had been good He had not had pneumonia, pleurisy, typhoid fever, malaria, rheumatic fever, chorea, tonsillitis, scarlet fever, diphtheria, otitis media or hernia He had had smallpox, measles, mumps, whooping cough and chickenpox He had had no operations or serious injuries

About the first of June a painful papular growth had developed on the alveolar margin of the lower jaw on the right His lower plate had seemed to irritate this growth, so that he had discarded his plate in the middle of June Soon after

this the area had ulcerated and steadily increased in size. About the middle of July there had appeared an external swelling over this area, which had grown more tender. This had fluctuated somewhat in size. He had worn his dental plates night and day since 1922, until the lower plate was discarded. His last dental extraction, eleven years before admission, had been in the area of the tumor.

He had not suffered from headaches, epistaxis, earache, sore throat, ocular infections or deafness. His vision had failed to some extent. He had not suffered from dyspnea, orthopnea, pain in the chest or heart, chronic cough, night sweats, hemoptysis or edema. His appetite had been good. He had had no pain after meals. He had not suffered from flatulence or gas. There was no history of nausea, vomiting, hematemesis, jaundice or tarry or clay-colored stools. He had had occasional hematochezia but no hemorrhoids and no nocturia. He stated that he had never had gonorrhea or syphilis. He had not fainted and had not been paralyzed.

Physical examination showed him to be well developed and well nourished. He was lying in bed in no apparent distress. The pupils were equal and regular. They reacted to light and in accommodation. The ocular movements were normal. There was no exophthalmos, nystagmus or lid lag. There was marked bilateral arcus senilis and considerable conjunctival injection, but no discharge. The vision was grossly normal. The ears and the hearing were normal.

There was no nasal discharge, obstruction or septal perforation or deviation. The mouth was edentulous. The tongue was slightly coated. The margins of the tongue were smooth and glossy. There was no deviation or tremor. The tonsils were atrophic. The pharynx was somewhat injected. The posterior pillars met above to form a V-shaped opening into the pharynx. The soft plate was rudimentary, and the uvula was missing.

There was an ulceration of the alveolar margin of the lower jaw on the right, extending over what had been the molar area. There was thickening of the margin of the jaw from side to side, as determined by intraoral examination, and marked induration extending into the cheek and to the upper jaw. All affected areas were very tender.

There was no tenderness of the frontal, antral or mastoid regions. There was no cervical or axillary adenopathy. There was slight inguinal glandular enlargement. There was no enlargement of the thyroid. There were no pulsations, masses, tracheal deviations or tugs.

The chest was symmetric. There were no tumors or deformities. There was slight costovertebral tenderness on the right but none on the left. There was no vertebral tenderness. There were numerous elevated nevi. Expansion of the lungs was equal and regular. The bases were mobile. The percussion, fremitus, breath, voice and whispered sounds were normal. There were no rales. The point of maximum impulse and the borders of the heart were within normal limits. There were no thrills or shocks. The sounds were of normal intensity, quality and duration. The pulmonic second sound was equal to the aortic. There were no murmurs. The blood pressure was 134 systolic and 80 diastolic. The pulses were equal and regular. There was no thickening or tortuosity of the peripheral vessels.

The abdomen was distended, so that a satisfactory examination was not possible. It was impossible to palpate any of the organs. No masses, hernias or pulsations could be felt. There was slight tenderness over the region of the gallbladder.

The external genitalia were normal. There were no tumors or deformities of the extremities and no varicosities of the legs. The quadriceps and biceps reflexes were present and active. External rectal examination revealed no abnormality. Internal digital examination revealed the right lobe of the prostate to be larger than the left. Both lobes were nontender and firm.

The provisional diagnosis was malignant disease of the right side of the lower jaw.



Fig. 11 (case 7)—Photomicrograph of a squamous cell carcinoma of the lower jaw.

The surgical consultant recommended a biopsy followed by radium treatment. The dermatologist advised surgical removal followed by high voltage roentgen therapy. He did not believe that radium would be satisfactory, because the disease was too advanced.

On August 11, with the region under local anesthesia induced with 2 per cent procaine hydrochloride, a section of tissue was excised and sent to the laboratory.

The pathologist reported that there were four pieces of soft, dark red tissue preserved in Zenker's solution. The largest piece measured 1 by 0.5 cm.

Microscopic sections showed areas of blood clot containing small, irregularly shaped groups of atypical epithelial cells and a small amount of loose, proliferating

fibrous tissue The cells were fusiform to polygonal and had a moderate amount of blue-staining cytoplasm with small to large fusiform to round nuclei Numerous mitotic figures were seen Many of the surface cells contained keratin, and in some areas a few flat keratinized cells covered the surface

The pathologist's diagnosis was squamous cell carcinoma of the lower jaw

The radiologist reported marked rarefaction of bone and destructive changes involving the posterior portion of the horizontal ramus of the mandible

On August 6 the laboratory reported the urine to be normal The value for hemoglobin was 80 per cent by the Dare test The erythrocytes numbered 4,950,000 and the leukocytes 10,000 per cubic millimeter, with polymorphonuclears 71 per cent, small lymphocytes 28 per cent and eosinophils 1 per cent The Wassermann reaction of the blood was negative The value for blood sugar was 61 mg and that for total protein 60 mg per hundred cubic centimeters The Wassermann reaction of the spinal fluid was negative

On August 16 the patient was discharged to a convalescent home for radium therapy

CASE 8—R F F, a white man aged 29, a farmer, was admitted to the hospital Aug 26, 1932, with a diagnosis of malignant disease of the jaw

His chief complaint was of a sore on the right side of the lower jaw

His mother was living and well at 48, and his father was living and well at 50 He had no brothers or sisters There was no history of familial diseases

He smoked two packages of cigarets each week He drank in moderation, but he had not used drugs He ate and slept well

He had been married at the age of 23 There was one child, 5 years old He had been divorced after three years of married life He had remarried at the age of 27 There was one child, 20 months old, by his second wife Neither of his wives had had any miscarriages

He had had measles, mumps, chickenpox, scarlet fever and whooping cough in childhood He had had severe influenza in 1918, but no complications or sequelae He had had gonorrhea at 18 years of age He had had no operations or injuries and no other previous illnesses

Ever since he was a boy he had had a tender lower lip This would often get dry and crack He had always lived a rugged life outdoors A year and a half before his admission to the hospital his lip on the right side had become sore again, and this time he had believed that he had a cold sore This had slowly increased in size for one year Then the sore had become hard and nodular The hardness had seemed to extend a considerable distance down into the tissues A physician had told him that this was syphilis, because the Wassermann reaction was positive He had started to take "shots" for this, taking a total of twenty-eight However, the sore had kept getting larger, so that four months before admission to the hospital he had noticed a "knot" just below the chin This also had increased in size On July 1 the lesion under the chin had become inflamed, and the physician had cut into it, releasing some pus About the middle of July he had gone to a laboratory, where a dark field examination was made and reported as revealing *Spirochaeta pallida* More injections had been given, without improvement, so that the patient had decided to enter a hospital Eleven months before admission he had had a small sore on the penis, about the size of a match head This had been hard at first and then had broken down, with a discharge of pus This sore had lasted two months It had become well without treatment There was no history of secondary syphilitic infection

When admitted he was suffering from almost constant headache, with considerable pain in the right mastoid and cervical region

General physical examination showed him to be well developed and well nourished. He was lying quietly in bed. He seemed of average mentality and apprehensive. His skin was moist.

On the right side of the lower lip was a large crater-like depression, crusted over with black material. The edges of the crater were raised and eroded. The tissues beneath were swollen and hard. Below the angle of the jaw was another ragged, depressed lesion similar to the one on the lip. Foul-smelling, tenacious white material exuded from both lesions. The swelling and the tumor mass extended up to just below the ear and down for 5 or 6 cm into the neck and also from the midline of the neck to the trapezius muscle. Lateral to the lesion on the lip there was a round, soft swelling about the size of a marble. This swelling was slightly reddened, warm and fluctuant.

The skull was of normal contour. There were no exostoses or points of tenderness except for the region just anterior to the ear, which was slightly tender. The pupils were round, regular and equal, they reacted normally. The scleras and conjunctivas were normal. The ocular movements were normal. The fundi were not examined. The ears and nose were externally normal. The teeth were in fairly good condition. The tongue protruded normally but was slightly coated. The tonsils were moderately hypertrophied, the right more than the left. The anterior pillars were moderately injected. The pharynx was granular in appearance. No postnasal discharge was noticed. The neck was normal except for the tumor and the lesion described.

The chest had a normal contour and was symmetric. The expansions were equal and of good quality. The heart was not enlarged to percussion. The point of maximum impulse was in the fifth space, inside the midclavicular line. There were no thrills. The sounds were of good quality, and there were no murmurs. The pulmonic second sound was greater than the aortic. The blood pressure was 130 systolic and 85 diastolic. The lungs were normal to inspection, palpation, percussion and auscultation.

The abdomen was of normal contour. There were no masses or points of tenderness. The liver and spleen were not palpated. There was no renal tenderness or pain on jarring. There was no dullness in the flanks.

There was a small white scar on the prepuce dorsally. The inguinal glands were palpable bilaterally. The external genitalia were otherwise normal.

The extremities were normal. The patellar, achilles biceps and triceps reflexes were present and hyperactive. The Babinski sign was negative. The cremasteric and abdominal reflexes were present.

The provisional diagnosis was squamous cell carcinoma of the jaw and lip with an old syphilitic scar on the prepuce.

Four urinalyses, performed from Aug 27 to Feb 3, 1933, revealed no abnormality. The value for hemoglobin was 80 per cent by the Dare test on Aug 27, 1932. This gradually dropped to 60 per cent on Feb 3, 1933. The erythrocyte count ranged from 3,710,000 to 5,060,000 per cubic millimeter during the same period. The leukocytes ranged from 10,350 to 14,450 per cubic millimeter and the polymorphonuclears, from 76 to 80 per cent. The small lymphocytes ranged from 13 to 23 per cent, and the eosinophils, from 1 to 2 per cent. The Wassermann reaction of the blood was negative.

A biopsy specimen taken from the right side of the lower jaw on Aug 26, 1932, consisted of five tiny pieces of soft dark red tissue. Under the microscope

the sections showed a thick layer of stratified squamous epithelium without a cornified layer. The basal cells were in one place continuous with an irregular mass of atypical squamous cells. There were several irregularly shaped masses of such cells, which varied greatly in size, shape and staining qualities. The majority of the cells were partially keratinized, and many of the groups contained more or less typical epithelial pearls near the central portions. However, in one place the cells formed strands of one or two cell widths. These were



Fig 12 (case 8) —Photomicrograph of another squamous cell carcinoma of the lower jaw

cuboidal or polygonal and stained bluish pink. Many lymphocytes, plasma cells, polymorphonuclear leukocytes and mucous glands were observed in the proliferating fibrous tissue stroma.

The pathologist's diagnosis was squamous cell carcinoma of the jaw.

The patient received high voltage roentgen therapy on September 2 and 3. The radiologist advised against more therapy for one month. He advised that the patient be discharged on leave, and this was done on September 4. However, the patient returned from leave on September 14, complaining of a throbbing pain in

his face and loss of sleep. He was given four roentgen ray treatments of the face and potassium permanganate packs to his jaw. He was discharged again for six weeks.

The patient returned from leave on October 13, complaining of great pain. He was worse than he had been before. He was given amytal compound and codeine sulfate for the pain and local treatment for the carcinoma. A dermatologist advised a powder of dextrose and lactose, to be applied locally as a deodorant. A general surgeon advised radium therapy and then operation. The powder definitely lessened the bad odor, and radium was applied on October 23. Fifty milligrams was used, screened with 2 mm of lead at a distance of 2 cm for twenty-four hours. This dose of 1,200 milligram hours was repeated on October 24, 25, 26, 27 and 28. He was also given calcium gluconate.

He was freer from pain for a time but gradually became worse. By December 5 the ulcer of the lip and that of the jaw had almost met. By January 5, 1933 he required $1\frac{1}{2}$ grains (0.09 Gm) of morphine sulfate a day for relief of his pain.

He gradually lost weight. The ulceration and necrosis increased. The emaciation and debility ended fatally on March 16. There was myocardial failure at the end.

CASE 9—A. H., a white American man aged 66, a farmer, was admitted to the hospital April 18, 1933, with a diagnosis of tumor of the jaw.

His chief complaint was of a tumor in the left side of the lower jaw, of one year's duration.

His mother had died at 43 of puerperal fever. His father had died at 67 from an unknown cause. He had one brother living and well at 74. One brother had died at birth, one from a fall which broke his neck and one from tuberculosis at the age of 32. He had three sisters living and well. One sister had died of malaria at 26, one in labor at 24, and one at 60 of an unknown cause. There was no family history of cancer, cardiac disorder, renal disorder, diabetes, hemophilia, gout or insanity.

The patient had been married for 31 years. He and his wife had thirteen children living and well. One child had died at the age of 5 months, of scarlet fever. His wife had died four years before his admission to the hospital, from carcinoma of the liver. He drank one cup of coffee a day but no tea. For five years before admission he had not used alcohol, but before that he had drunk excessively. He had not used tobacco for the preceding four years, but he had previously smoked a pipe and cigarettes. He had not used drugs. He had had measles, mumps, whooping cough, chickenpox, scarlet fever and malaria by the time he was 30. He had not had smallpox, diphtheria, typhoid fever, pneumonia or rheumatic fever. He had had no operations. A horse had jumped on his chest fourteen years before admission and fractured his ribs and sternum over his heart. His lower lip and left ear had been frozen eighteen years before.

About ten years before admission he had noticed a small papule in the right side of the lower lip. When he shaved this would bleed and then reappear. Iodine had been applied at first, but this had caused excruciating pain. The papule had gradually become larger, and the tissues in the lower lip had become indurated. There had been a constant dull pain present, and at times the pain had been severe enough to keep him awake at night. Poultices had been applied, and soon cheesy material had exuded from the growth. Glandular enlargements had not been noticed at any time.

His condition had not improved, so that after eight months he had gone to a "woman healer" She had given him a course of treatments which consisted of hypodermic injections into the growth and salves This had caused severe pain, and red streaks had appeared, going to the external meatus of the right ear and beneath the ear down to the chin The glands in front of the right ear and below the ear had become enlarged and tender This had disappeared after the third day of treatment, and at the end of the ninth day the indurated tissue and papule had sloughed away In a few days the tissues had healed, and the patient had been relieved of his symptoms

About two years before admission the patient had noticed a small papule, similar to the first one, in the left side of the lower lip This small growth had cracked, when picked, it bled and later reformed The patient had attempted to treat this himself with the injections and salves, but the growth had not entirely disappeared About the same time the patient had noticed a small gland under the left side of the lower jaw This was tender to pressure and gradually increased in size In August 1932 he had gone to a "radium doctor" in another state Eight needles had been implanted for three hours These had then been reinserted, with four more, into the lip and the inner side of the left cheek for another six hours Sloughing had occurred about three days later, and the swelling had disappeared This had continued to slough for about two months The gland under the jaw had not disappeared but had gradually become larger and more indurated until the latter part of December 1932, when the growth had become attached to the jaw bone

The skin around the growth had also become attached to the growth, so that when the patient stretched his neck the skin became drawn The growth was painful, and there was a dull, throbbing, constant pain at the time the pain was severest The patient had not been able to sleep The pain was localized under the jaw and did not radiate

General physical examination showed the patient to be well developed and well nourished He was sitting quietly, in no distress He was cooperative and intelligent The skull was symmetric, and there were no exostoses The scalp was clean, and there were no scars He had a very scanty growth of gray hair The pupils were irregular but equal They reacted to light and in accommodation There was no lagging of the lids, strabismus, exophthalmos or nystagmus The conjunctivas were injected at the outer canthi There was a pterygium of the left eye at the medial limbus The nose was externally normal There was no discharge The ears were externally normal There was no discharge, and there were no tophi

The mouth was edentulous The tonsils were small and injected The pillars were injected There was no postpharyngeal discharge The tongue was clean and moist It protruded in the midline, without tremor The lower lip showed linear scars in the lateral aspects, and the lip was contracted The mucous membrane over the left cheek was contracted near the angle of the mouth, and it was tender

Below the left side of the jaw there was an indurated mass about the size of a baseball, which was adherent to the jaw bone and to the skin The mass was immovable and tender on pressure It extended from the lower jaw to the median line below the chin There was no cervical adenopathy The thyroid gland was not palpable

There was depression of the ribs over the precordial area The respirations were equal and regular The breath sounds were normal There were no rales

The lungs were resonant throughout. The heart beats were of fair quality. There was a soft systolic murmur, heard best at the apex. This was not transmitted to the axilla or to the back. The aortic second sound was greater than the pulmonic. The point of maximum impulse was heard in the sixth interspace, outside the midclavicular line. The blood pressure was 160 systolic and 74 diastolic.

The abdomen was symmetric. There were no masses. There was no tenderness or rigidity. The liver and spleen were not palpable or tender. The kidneys were not palpable and were not tender when the back was jarred.

The fingers were not cyanotic and were not clubbed. There was no edema of the lower extremities and no tremor. The axillary and inguinal lymph nodes were not abnormally enlarged. The deep reflexes of the upper extremities were equal and normal. The upper and lower abdominal reflexes were sluggish. The cremasteric reflexes were present. The knee jerks were equal and normal. The achilles reflexes were equal and normal. The Babinski and Romberg signs were negative.

The provisional diagnosis was malignant disease of the jaw.

On April 20 the laboratory reported analysis as giving negative results. The value for hemoglobin was 80 per cent by the Dare method. The erythrocytes numbered 4,900,000 and the leukocytes 8,500 per cubic millimeter, with polymorphonuclears 68 per cent and small lymphocytes 30 per cent. The Wassermann reaction of the blood was negative.

The radiologist found no definite evidence of invasion of bone by tumor on April 20.

The surgeon who saw him believed the tumor inoperable and advised irradiation.

High voltage roentgen therapy was administered three times between April 20 and 29. The first area covered was 10 by 10 cm. The second and third were each 20 by 20 cm. The distance of the tube was always 58 cm and the spark gap 180 kilovolts, using 30 milliamperes. The filter was 5 mm of copper and 2 mm of aluminum. The treatments all lasted ten minutes and were applied to the left side of the lower jaw.

The patient was discharged on leave on April 29 to return in four weeks, but he did not return. A biopsy was not performed. The clinical diagnosis was carcinoma of the jaw.

CASE 10—J. P., an Italian schoolboy aged 8 years, was admitted to the hospital on Nov. 26, 1933, with a provisional diagnosis of tumor of the mandible.

His chief complaint on admission was of a swelling under the right side of the lower jaw, present for one and a half months.

His father and mother were living and well. He had four sisters and two brothers, all living and well. There was no history of familial diseases. The patient had not had measles, mumps, scarlet fever, diphtheria or other childhood diseases.

Two or three weeks after the swelling below the jaw had been noticed, a lower tooth had been extracted. This had not lessened the swelling below the jaw. After the extraction the patient had had nose bleed about once a week, usually at night. After the hemorrhage the father had thought that the boy felt better. The patient had not suffered much pain.

General physical examination showed him to be normally developed and in no acute distress.

The skull was symmetric and smooth. The scalp was clean. The pupils were dilated, equal and regular. They reacted to light and in accommodation. The

ocular movements were normal. The conjunctivas were normal. The ears were externally normal. The nose was externally normal except for some crusting in the anterior nares. The teeth and the tongue were clean. The tonsils were normal. The pharynx was injected, and there was a thick postnasal discharge.

In the neck there was a large, hard swelling below the right side of the lower jaw, about the size of an egg. It could be felt in the floor of the mouth, and it seemed to be attached to the bone. It was not tender. The skin was normal in color over the tumor. The thyroid was not enlarged. There was one large gland at the angle of the jaw.

The chest expansion was good and was equal on the two sides. The lungs were resonant throughout, and the breath sounds were normal throughout. There were no rales. The heart was of normal size. The sounds were of good quality. There were no murmurs. The pulmonic second sound was greater than the aortic. The pulse was good.

The abdomen was flat and muscular. There was no tenderness or rigidity. No organs or masses were palpable. The genitalia were normal for an 8 year old boy.

There were no deformities of the back and no tenderness. The extremities were normal and well nourished. There was no edema. The reflexes were normal.

The clinical diagnosis was probable sarcoma of the jaw. Fibroma, giant cell tumor and osteoma were also considered.

Urinalysis on November 27 gave negative results. The erythrocytes numbered 4,160,000 and the leukocytes 7,650 per cubic millimeter, with polymorphonuclears 63 per cent, small lymphocytes 32 per cent and endothelial cells 5 per cent. The hemoglobin was of normal concentration. A pharyngeal smear showed no evidence of diphtheria.

The radiologist on November 28 reported extensive erosion of the lower aspect of the right horizontal ramus of the jaw, combined with evidence of bony spicules extending from the same area. This suggested bony involvement of the tumor. He stated the opinion that the tumor was probably an osteogenic (periosteal) sarcoma. He found no evidence of tumor invasion or other pathologic change in the chest.

On December 1, with the boy under general anesthesia, a hard, firmly fixed tumor the size of a large walnut, projecting from the inferior border of the right lower jaw near the center and just anterior to the facial artery, was removed. The tumor involved the outer layers of bone, which seemed to be more or less expanded. There were a number of enlarged submaxillary lymph nodes within and surrounding the submaxillary salivary gland. The tumor extended up on the internal surface of the bone as far as the mucous membrane of the mouth and involved the periosteum to the same point.

The tumor was chiseled away, with a considerable amount of the bone, during this operation the floor of the mouth was opened. The submaxillary gland and all of its lymph nodes were removed.

The pathologist reported that the tumor consisted of a very firm, irregularly rounded mass 7 by 5.5 by 5.3 cm. The external surface was red and covered with tags of adipose tissue and some glandular material. In one end there were several masses of bone. The largest piece of bone was 4 by 1 cm. The cut surface showed firm, whitish tissue composed of bundles of fibrillar material. There were several small lymph glands, which appeared soft and red and had a fairly homogeneous cut surface. There was another mass, yellowish red, soft and lobulated, measuring 3 by 2.5 by 0.3 cm. This appeared to be a submaxillary gland.

Microscopic examination showed that the main portion of the tumor was composed of interwoven masses of fibrillar connective tissue, the intercellular matrix of this tissue was very dense and in areas seemed to have undergone a great deal of degeneration. The cells had elongated, spindle-shaped adult type nuclei, though there appeared to be a greater ratio of nuclei to matrix than in ordinary connective tissue. Mitotic figures were rare. The tumor tissue had invaded muscle and adipose tissue, many of the muscle fibers having undergone degeneration.

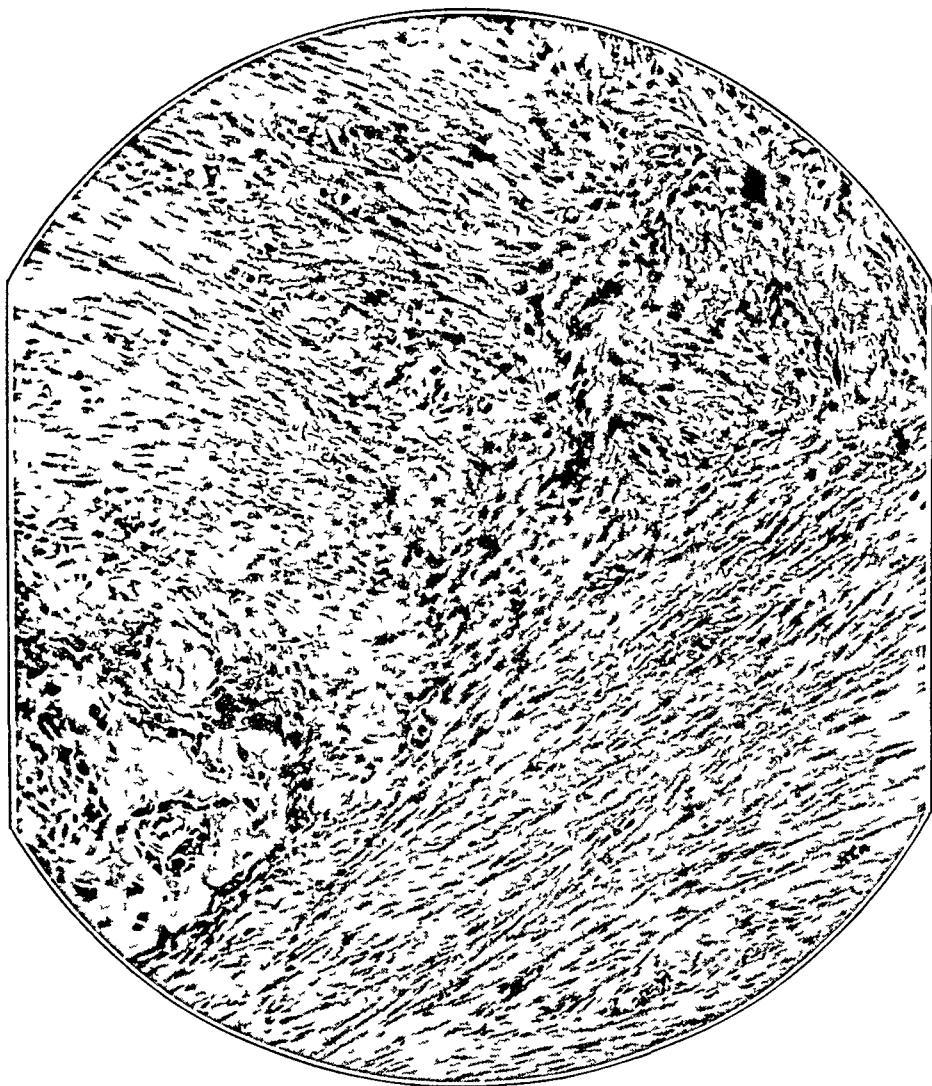


Fig 13 (case 10) —Photomicrograph of a fibrosarcoma of the jaw

There were also spicules of bone in the tumor, which appeared to be newly formed. Portions had lamellar structure, and the marrow cavities were occupied by tumor tissue. Osteoblasts were numerous. The tumor tissue was supplied with a small number of thin-walled blood vessels. The lymph nodes had thickened capsules, and in some the connective tissue about the vessels and in the septums seemed greatly thickened. In some there were slight edema and fairly marked hyperplasia of the follicles. Section of the submaxillary gland revealed nothing remarkable.

The pathologist's diagnosis was fibrosarcoma of the jaw with hyperplasia of the cervical lymph nodes.

The wound healed uneventfully after the operation, and the opening into the mouth closed

High voltage roentgen treatment was started on December 18 and ended on December 23

The patient was discharged on leave on December 24. He returned on Jan 22, 1934. His progress while on leave had been uneventful. His general physical condition was good, and the wound was healed. The mandible felt rough on the right side. He was given more high voltage roentgen therapy from January 22 to 27. He was discharged in a satisfactory condition on January 31, to return in eight weeks for further treatment.

He returned from leave on April 8, in good condition. There was no soreness in the region of the jaw. He received a series of four treatments to the right side of the jaw. He was discharged again on leave on April 13, as improved.

He returned for reexamination on June 15. The radiologist could find no evidence of recurrence. He was again discharged on leave on June 19.

CASE 11—F. B., a white American man aged 57, a miner, was admitted to the hospital Dec 11, 1934, with a diagnosis of tumor of the jaw, probably malignant.

His chief complaint was of dull intermittent pain in the right side of the lower jaw for the preceding eight weeks. His father and mother were dead. He did not know at what age they had died or the cause of death. Two sisters had died at the ages of 33 and 34, of unknown cause. He had no brothers. There was no family history of diabetes, cancer, renal disease, cardiac disease or mental or nervous disease.

He drank two to four cups of coffee per day and smoked one or two packages of cigarets each day. Prior to four years before admission he had been a heavy drinker of alcoholic liquor. He slept well, and his bowels were regular. He had been married for twenty years. His wife had excellent health. There were no children.

He had had chickenpox, mumps, measles, German measles and whooping cough in childhood. He had not had diphtheria or scarlet fever. He had had pneumonia in 1905 or 1906 while working in lead and zinc mines. He stated that he had never had gonorrhea or syphilis. He had not had any serious accidents or operations. His teeth had all been removed one month before he was admitted to the hospital.

Two months before admission he had noticed a sensation in the right side of the lower jaw, which he described as a dull toothache. However, the tooth had been removed. The pain had been intermittent and dull. He had seen a physician, and a roentgenogram had been made. The bone had appeared cloudy. The physician advised removal of all of his teeth. The teeth had been extracted by a dentist. The physician had scraped the jawbone to remove tissue. This had been sent to Chicago for an examination. The laboratory had reported an osteoma, but his physician had sent him to the Colorado General Hospital for observation and treatment. He had a small hernia of thirty-five years' duration. He had lost 15 to 20 pounds (6.8 to 9.1 Kg) the month before admission, which he attributed to loss of appetite.

Physical examination showed him to be gray haired and not acutely ill. There was no dyspnea, orthopnea or edema. There were no scars, and there was no tenderness of the scalp. There were no deformities of the skull. The scleras and conjunctivas were moderately injected. The pupils were equal and regular and reacted to light and in accommodation. The ears were externally normal. There was some secretion in the nose. The septum deviated to the right. There was

no perforation. The tongue tended to deviate to the right but with effort could be protruded in the midline. All of the teeth had been extracted except a small fragment of the left upper incisor. The gums had not completely healed. The posterior region of the right inferior gum was occupied by a reddened growth with patches of exudate. This growth was about 2.5 by 1 cm and was elevated above the gingival margin. In the adjacent cheek there was a patch of leukoplakia. The tonsils were small. The pharynx was slightly injected. There was some postnasal discharge. There was no enlargement of the thyroid. There was no tracheal tug or deviation. The submandibular and submaxillary glands were enlarged. Both were firm but not tender. The mandible was tender at the angle on the right side.

The spine was normal. The expansion of the chest was equal on the two sides. The lungs were clear and resonant. The heart was not enlarged to percussion. The sounds were somewhat distant, but no murmurs were heard. The rate and rhythm were regular. The pulse was of good quality. The blood pressure was 140 systolic and 90 diastolic.

There was spasm of the voluntary abdominal muscles. There were no masses and no tenderness. The liver, spleen and kidneys were not felt. The genitalia were normal. The reflexes and extremities were normal.

The provisional diagnosis was carcinoma of the mandible.

On December 12 urinalysis gave negative results. The value for hemoglobin was 15.8 Gm by the Sahli test. The erythrocytes numbered 4,780,000 and the leukocytes 9,500 per cubic millimeter, with polymorphonuclears 71 per cent, lymphocytes 24 per cent, endothelial cells 2 per cent and eosinophils 3 per cent.

The radiologist on December 14 reported extensive bone rarefaction and destruction, apparently due to invasion by malignant tumor, involving the right side of the inferior maxilla.

On December 14, with the patient under avertin with amylene hydrate and intratracheal ether anesthesia, the jawbone was curetted.

The pathologist reported that the specimen removed consisted of five pieces of soft tissue, the largest of which measured 4.5 by 3 by 2 cm. The specimens were similar in appearance. These were hemorrhagic, rough fragments, apparently of fibrous connective tissue. One fragment was roughened by a piece of cartilage.

The microscopic specimen consisted of sheets, cords and nests of epithelial cells with large oval and round hyperchromatic nuclei which had invaded the surrounding connective tissue and muscle. Many mitotic figures were observed, and there was pearl formation in several of the epithelial strands. The connective tissue was abundant and was infiltrated with polymorphonuclears, lymphocytes and monocytes. There were several areas which showed muscle bundles undergoing atrophy. At one corner of the specimen there were a few spicules of what was apparently newly formed bone. There was little calcium, and the spicules were surrounded by osteoblasts.

The pathologist's diagnosis was squamous cell carcinoma of the jaw (point of origin not determined).

On December 20 a series of four high voltage roentgen treatments was started. The patient was discharged on leave on December 24 and returned on Jan 22, 1935. When he was readmitted the wound in the jaw had broken down and was discharging. It had also opened inside the mouth. The wound was opened and a drain inserted. Hot packs were applied. He received more high voltage roentgen therapy and was again discharged on leave on January 28. He returned from his second leave on March 1, but he was sent to the Good Samaritan Hospital. He

was finally discharged on April 16. He had received a total of eight roentgen treatments from Dec 20, 1934 to Jan 28, 1935. He was discharged as unimproved.

CASE 12—B F, a Mexican aged 47, a farmer, was admitted to the hospital March 23, 1935, with a diagnosis of probable malignant tumor of the right side of the lower jaw.

His chief complaint was of pain and swelling of the right side of the face for six months.

His father had died at 75 of an unknown cause. His mother had died at 35 of cardiac or renal disease. He had two brothers and one sister living and well. There was no history of tuberculosis, cancer, syphilis, diabetes or nervous or mental disease in the family. His wife had died in childbirth nineteen years before his admission to the hospital. There had been no other children. He had had smallpox at 9 years of age, but no other childhood diseases that he knew of. He had not had any serious accidents or illnesses. He stated that he had not had syphilis. He had had gonorrhea thirty-two years before. He had been treated by a "druggist doctor" and had had no more trouble.

His recent illness, with swelling in the right side of his face, had led him to consult a dentist, who extracted eighteen of his teeth. This failed to relieve either the pain or the swelling. The pain was periodic and very sharp. It was well circumscribed and did not radiate. After extraction of the teeth he had had too much saliva.

Physical examination showed him lying quietly in bed but suffering some pain in the right side of the lower jaw.

The scalp was sparsely covered with fine, light hair. The scalp was clean, and there were no exostoses. The pupils were equal and regular. They reacted to light and in accommodation. The ocular movements were normal. The ears were externally normal. The patient complained of a peculiar sensation in his right ear, but his hearing was not impaired. All the teeth above and below on the right and most of those on the left had been removed just before he was admitted to the hospital. Examination of the mouth was unsatisfactory because he was unable to open his mouth more than a $\frac{1}{2}$ inch (12 cm). There was a hard swelling on the right, extending well into the oral cavity. The tongue protruded in the midline without tremor. The pharynx and tonsils could not be seen. There was an excess of saliva. The patient was forced to expectorate every few minutes. The swelling on the right side was about the size of a baseball. It was tense and painful to the touch.

The thyroid was not enlarged. There was some adenopathy on both sides of the neck. The lymph nodes were not tender.

The excursions of the chest were equal on the two sides. The patient was thin and not well developed. The lungs were resonant throughout. There were no rales. The breath sounds were normal. The heart sounds were of good quality. There were no murmurs. The pulmonic second sound was greater than the aortic. The rate was 80. The point of maximum impulse was within normal limits. The blood pressure was 110 systolic and 70 diastolic.

There were no masses in the abdomen and no areas of tenderness or rigidity. The liver and spleen were not palpable. The extremities were grossly normal. The prostate was slightly enlarged. It seemed to be of normal consistency. The reflexes were normal.

The provisional diagnosis was carcinoma of the right side of the jaw with osteomyelitis.

On March 25 the laboratory reported urinalysis as giving negative results. The value for hemoglobin was 115 Gm by the Sahli test. The erythrocytes numbered 4,030,000 and the leukocytes 10,500 per cubic millimeter, with polymorphonuclears 80 per cent, lymphocytes 18 per cent and endothelial cells 2 per cent.

The radiologist reported very extensive destruction of the right mandible, apparently caused by malignant disease rather than by osteomyelitis.

The patient received a series of high voltage roentgen treatments between March 25 and April 11. He was discharged on leave on the latter date to return for radium treatment in four weeks. He was discharged off leave on July 14. A biopsy was not performed.

CASE 13—L. H., a white housewife, aged 79, was admitted to the hospital on Aug. 27, 1935, with a malignant tumor of the right side of the jaw.

Her chief complaint was of the tumor and of bleeding from an ulcer of the tumor for three years. Her father had died from an accident when she was an infant. Her mother had died from typhoid at 50. Three of her brothers had died from an unknown cause. Three sisters had died, also from an unknown cause. One sister had consumption. There was no family history of cancer, cardiac, renal, allergic or mental disease. The patient had suffered from mild bronchial asthma for many years.

She had had the usual childhood diseases. She had had typhoid fever at 13 years of age but no other serious illness. She had not sustained any injuries.

About eighteen years before admission the patient had noticed a small, hard lump on the right side of the jaw, about the size of a small pea. This had oozed a small amount of blood at various times, but it had not been painful. It had disappeared but had reappeared three years before admission, at which time it had begun to enlarge and finally had developed into a firm, ulcerated mass. This had become progressively more painful. During the week before admission there had been considerable surface bleeding.

General physical examination revealed the patient to be very emaciated, small and in some apparent distress but fairly cooperative. The head was of normal contour, and the scalp was covered with coarse gray hair. The ears were externally normal. The nasal septum deviated to the right. The mouth was edentulous. The mucous membranes were pale and the tongue smooth. The pharynx was not injected. The tonsils were not visible. The scleras and conjunctivas were moderately injected. There was an arcus senilis of each eye. The pupils were equal and regular. They reacted to light very sluggishly. There was a beginning opacity in the right lens.

There was an ulcerated mass in the right side of the neck, just below the jaw. This extended from the angle of the jaw to about 2 inches (5 cm) from the point of the jaw. There was no stiffness of the neck. The cervical lymph nodes on the right were enlarged to the supraclavicular area. The thyroid was not palpable.

The thorax was somewhat rounded and was symmetric. The respiratory movements were shallow and equal. The breasts were atrophic. There were no masses. The bronchial breathing was generalized in the parenchyma. Coarse rales were heard over the bases of both lungs and the apex of the right. The heart was not enlarged to percussion. The sounds were of moderate strength, and the rhythm was regular. The rate was 90. There were no murmurs. The blood pressure was 158 systolic and 80 diastolic. The peripheral vessels were tortuous and moderately sclerosed.

The abdomen showed the stria of a former pregnancy. There was a symmetric enlargement in both lower quadrants. There were no palpable masses. There was shifting dullness. There was no tenderness. The genitalia were not examined.

The extremities were very atrophic. There was scarring over each tibia. There was a firm mass about the size of an English walnut on the left thenar eminence, which was slightly tender. Both the axillary and inguinal lymph nodes were moderately enlarged. Those in the axillae were about the size of a small walnut. The reflexes were equal and present throughout, but sluggish. The Babinski and Gordon signs were negative.

The clinical diagnosis was carcinoma of the right cervical region with beginning generalized metastasis.

On August 28 the laboratory reported the urine to be normal. The value for hemoglobin was 8.1 Gm by the Sahli test. The erythrocytes numbered 3,780,000 and the leukocytes 14,500 per cubic millimeter of blood, with polymorphonuclears 84 per cent and lymphocytes 16 per cent.

The consultants who saw the patient believed that the tumor was inoperable, but they advised high voltage roentgen therapy for relief of pain. They believed that the prognosis was hopeless. Local applications were used for relief from the odor and for drying. She received five high voltage roentgen treatments and was discharged on leave for one month on September 10.

She returned on Feb. 20, 1936. Reexamination revealed a moderate amount of induration at the site of the lesion. There was moderate discharge from the surface. The radiologist believed that further roentgen therapy should be deferred for another month, and the surgeon concurred in this. The patient was advised to return on March 23.

CASE 14.—F. J., a white schoolgirl aged 16, was admitted to the hospital April 7, 1937, with a diagnosis of probable dentigerous cyst of the jaw.

Her chief complaint was of a swelling in the jaw for seven months before admission. She had suffered from mild sore throat occasionally and from earache.

Examination showed a firm swelling, not movable below the lower lip. This extended from the midline over to the right side as far as the angle of the jaw. The cervical lymph nodes were nodular and enlarged. The tonsils were enlarged, and the anterior pillars were red.

The heart and lungs were normal. The blood pressure was 125 systolic and 75 diastolic.

On April 8 urinalysis gave negative results. The value for hemoglobin was 10.5 Gm by the Sahli test. The erythrocytes numbered 4,250,000 and the leukocytes 6,900 per cubic millimeter, with polymorphonuclears 44 per cent, lymphocytes 55 per cent and eosinophils 1 per cent.

The radiologist found no evidence of metastasis in the chest or in the bones.

The surgeon believed that the tumor was an adamantinoma. He made a gingival incision from the right second molar to the midline. A hard, vascular, bony tumor was curetted away from the body of the mandible. Thirty milligrams of radium was inserted. This was screened with 0.5 mm of lead. The cheek was screened with $\frac{1}{8}$ inch (0.32 cm) of gauze. She received 720 milligram hours of radium. The operation was done with the region under local anesthesia.

The pathologist said that the specimen measured 2 by 2 by 1 cm and was about the size and color of a raspberry, with a thin rim of bone partially encapsulating it and closely adherent to its surface. There were also many small pink amorphous fragments of bone, some of which had bits of the larger raspberry material adherent to its surface.

The microscopic sections consisted mainly of cellular young fibrous tissue with myriads of giant cells scattered through it. About the periphery was an uneven

rim of new bone formation, evidenced by osteoblasts. The marrow spaces were composed of coarse fibrous tissue occasionally infiltrated with a few round cells.

The pathologic diagnosis was giant cell tumor or epulis of the jaw. This is not malignant except for local bone destruction.

The patient was discharged to the outpatient clinic on April 11.

She returned for the removal of a spicule of bone with the region under local anesthesia on June 16. Her recovery was otherwise uneventful.



Fig 14 (case 14) —Photomicrograph of a giant cell tumor of the jaw

CASE 15—F P M, a white man aged 80, a rancher, was admitted to the hospital Jan 27, 1938, with a diagnosis of tumor of the mandible.

His chief complaint was of a swelling in the right side of the lower jaw and neck.

His father had died at 96 from erysipelas. His mother had died at 60 or 70 from an unknown cause. He had lost one brother at 36 from typhoid and another at 40 from an unknown cause. He had lost track of a sister. There was no family history of cancer, tuberculosis, diabetes, heart disease, renal disease, allergy, insanity or apoplexy.

Physical examination revealed him to be well developed but emaciated. He was lying quietly in bed and complaining of pain in the jaw. There was induration extending from the jaw down into the neck. There was a healed scar just at the jaw line. This was tender to palpation and prevented opening the mouth well. The skull and scalp were normal. The pupils were small and regular, but the right was the larger. The vision was very poor. The membrana tympani were retracted. The nose was injected. The tonsils were atrophic. The mouth was edentulous. There were no dental plates. The right gum line was white, hard and sore.

The chest was symmetric. The expansion was free and equal. The lungs were dull. There was bronchial breathing at the apex of the right lung and at the hilum of both lungs. The lower lobes were hyperresonant. The heart sounds were very faint. The heart was small to percussion and auscultation. There were no murmurs. The rate was normal. The blood pressure was 140 systolic and 40 diastolic.

The abdomen was scaphoid and smooth. It was tender along the course of the colon, with palpable, movable fecal masses and gas. There was no distention or rigidity. The extremities were emaciated, but the function was normal. The right testicle was large but soft. The prostate was small and firm, with a palpable median bar. The reflexes were all present and normal.

The clinical diagnosis was neoplasm of the right side of the jaw.

The laboratory reported the following reactions: pus, 2 plus; red cells, 2 plus; and granular casts, 1 plus. Urinalysis otherwise gave negative results. The value for hemoglobin was 13.4 Gm by the Sahli test on January 28. The erythrocytes numbered 5,030,000 and the leukocytes 9,400 per cubic millimeter, with polymorphonuclears 68 per cent, lymphocytes 30 per cent and endothelial cells 2 per cent. The basophils showed an occasional basket shape.

The radiologist on January 28 found the heart to be of normal size. The apex of the right lung was not clear but the parenchyma appeared clear.

The patient received palliative treatment on account of his senility. He was discharged on leave on February 3 for thirty days. He died on March 3.

CASE 16—W. R. F., a white boy aged 2 weeks, was admitted to the hospital on Dec. 10, 1937, with an undiagnosed tumor of the lower jaw.

The chief complaint of the mother was that the baby had been vaccinated against smallpox on November 26 and had had a very severe reaction. The vaccination was on the inner surface of the right arm. There was a large open ulcer without a scab. The baby had nursed well and had apparently gained weight. He had been very irritable, but he had not cried much and had slept well. The mother had noticed a small tumor on the anterior inferior margin of the gum.

General physical examination showed that the baby did not appear acutely ill. The eyes, ears, nose and throat were normal. There was a tumor 1.5 cm in diameter protruding from the lower gum at the midline in front.

The chest was clear to auscultation and percussion. The heart was normal. The cord was off, but there was some infection. The vaccination reaction under the right arm was severe and about 6 cm in diameter. It was without a scab except a little around the edge.

The laboratory reported the blood and urine normal on December 11.

The surgeon who saw the baby in consultation believed that the tumor was an epulis and advised observation for a time before operation.

The vaccination wound and the infected umbilicus were treated with hot boric acid compresses. These were followed by 95 per cent alcohol dressings.

The radiologist reported no evidence of invasion of bone or of a tooth in the tumor mass

The baby was discharged on December 15, to return for reexamination after he was old enough to be weaned

CASE 17—R A P, a white man aged 60, unemployed, was admitted to the hospital on Oct 17, 1937, with a tumor of the jaw

The chief complaint was of pain and swelling of the lower jaw

Six and one-half months before admission he had first noticed a mass the size of an acorn on the right side of the lower jaw This was tender and painful when he entered the hospital One month before admission the swelling had greatly enlarged, to cover the body and ramus of the jaw as far as the midline He had been eating a meal when he had felt something snap This had been followed by very sharp shooting pain in his jaw and the side of his face every time he had tried to talk or to move his jaw The next day he had consulted his physician, who had examined the tumor roentgenographically and advised removal On October 4, his physician had removed the tumor and had sent him to the Colorado General Hospital for irradiation The pathologist who sectioned and examined the tumor had reported a squamous cell carcinoma

The patient's father had died at 77 from disease of the kidney and bladder His mother had died at 80 from old age He had four brothers and one sister living and well He had lost one brother at 50 from miner's consumption The patient had had tuberculosis for fifteen years There was no family history of cancer, diabetes, heart or renal disease (except in the case of the father) or nervous or mental disease His wife had died at 69 from an unknown cause He had one daughter living and well His wife had not had any miscarriages or stillbirths He had used alcohol occasionally He had smoked a pipe five or six times a day and had done so for years Before he began smoking a pipe he had chewed tobacco He had had measles, pertussis, pneumonia and typhoid in childhood He had not had any other diseases

In 1915 the patient had been coughing, raising sputum, having night sweats and losing weight and strength His physician had made a diagnosis of pulmonary tuberculosis For five or six years before his admission to the hospital his cough had decreased, but the night sweats had continued His weight had been about the same At times his sputum had been blood streaked

In 1931 he had noticed an ulcerated sore on the left side of the lower lip He had had this removed several months later It had returned in 1933 He had had it removed a second time He denied that he had had venereal diseases

General physical examination revealed him to be fairly well developed and well nourished He was sitting upright in bed, holding his jaw in both hands, apparently in acute distress whenever he attempted to move it

The skull was symmetric There were no exostoses, masses or areas of tenderness The scalp was clean The hair was white and of moderate texture There was no nystagmus, strabismus, exophthalmos or lid lag The pupils were equal, round and regular They reacted to light and in accommodation There was an arcus senilis The fundi were essentially normal The ears were free from tophi and discharge The drums were normal The nose was free from septal deviation, perforation, obstruction or discharge

In the mouth there was a mass the size of a hen's egg on the right mandible near the angle There was induration of the floor of the mouth in the submaxillary region No crepitus was felt The mouth was edentulous The tongue protruded in the midline without tremor The pharynx was normal In the neck

there was a small chain of palpable anterior cervical lymph nodes on the right. The thyroid was not enlarged to palpation. The trachea was in the midline.

The chest was symmetric. The expansions were good and equal. There was moderate scoliosis to the right. There was slight dullness to percussion at the apex of the right lung, with bronchovesicular breathing which was almost bronchial in places. Rales could not be heard. The remainder of the lungs was clear. The apical impulse of the heart was visible and palpable in the fifth left space, at the midclavicular line. There was no enlargement to percussion and no thrills. The rate was 82, and the rhythm was regular. The tones were of fair quality. There were no murmurs. The aortic second sound was greater than the pulmonic. The blood pressure was 130 systolic and 85 diastolic.

The abdomen was scaphoid and tympanic. There were no scars. The liver, spleen and kidneys could not be felt. There were no masses. There was no tenderness and no spasm. The external genitalia were normal. The extremities and reflexes were normal.

The clinical diagnosis was carcinoma of the right side of the inferior maxilla, with fracture and possibly superimposed chronic osteomyelitis.

The laboratory reported that urinalysis gave negative results on October 9. The value for hemoglobin was 132 Gm by the Sahli test. The erythrocytes numbered 4,100,000 and the leukocytes 9,000 per cubic millimeter, with polymorphonuclears 69 per cent, lymphocytes 28 per cent, endothelial cells 2 per cent and eosinophils 1 per cent. The Wassermann test of the blood and the Eagle flocculation test gave negative results.

The radiologist on October 18 reported extensive bone rarefaction and destruction combined with a marked osseous defect in the right ramus of the mandible, probably due to osteomyelitis following surgical intervention and pathologic fracture. The radiologist believed that the bone rarefaction might also be due to tumor invasion. He found marked kyphoscoliosis of the dorsal portion of the spine. There was considerable fibrosis in the hilum and in the bronchial system but no evidence of intrathoracic invasion of tumor or other pulmonary parenchymal pathologic process. There was some widening of the upper mediastinum, possibly due to aortitis. The costophrenic angles were clear.

The surgeon who saw him injected 2 cc of 95 per cent alcohol into the mandibular branch of the fifth nerve on the right, by way of the cheek, just below the foramen ovale, with apparently perfect results. He recommended repeating the injection if necessary. This gave the patient so much relief that it was not thought advisable to start roentgen or radium therapy at once. He was discharged to a convalescent home on November 3.

He returned to the Colorado General Hospital on November 15 for more care. The surgeon who saw him resected the right side of the inferior maxilla with the patient under avertin with amylene hydrate anesthesia followed by cauterization. He made an elliptic incision wide of the scar and the area of cancerous infiltration beneath the skin of the right side of the inferior maxilla. The tumor was distinctly outlined. It extended to the bottom of the transverse process of the hyoid bone, involving all the deep structures above the hyoid bone. The posterior belly of the digastric and that of the stylohyoid muscles were excised. The jaw was separated to the right of the midline and excised, with the adherent tissue, to the point of fracture. This was just in front of the angle. All the tissue was thoroughly cauterized and coagulated. The posterior, diseased part of the jaw bone was removed. The stump of the bone was covered with wax. The mouth was

opened, and all the infiltration to the midline below the tongue was coagulated. The mucosa was closed and a drain made coming out near the posterior angle, and the skin was closed with dermal sutures.

The pathologist reported on November 19 that the gross specimen consisted of three pieces of tissue. The largest was 6 by 3 by 1.5 cm and consisted of hard, yellow bone, attached to which was red, beefy muscle, dark red mucous membrane and a tag of skin 2 by 0.5 cm. Another piece of bone, 2 by 2.5 by 1 cm, had some muscle and tendon attached to it. There were two other pieces of rubbery red, gray and yellow tissue measuring 2 by 1 by 1 cm and 2 by 0.5 by 0.5 cm respectively.

Microscopic examination showed a few stretches of thickened stratified squamous epithelium along the surface. Elsewhere the epithelium was replaced by wildly growing cords, plaques and whorls of epithelial cells with indistinct cell borders. The nuclei of the cells were large and irregularly oval or round. The chromatin material was irregularly clumped and darkly stained. Mitotic figures were numerous among these cells. The cells invaded a dense fibrous connective tissue arranged in a septum-like fashion. Many epithelial pearls were present. The mandibular bone was invaded by these whorls of cells, which were pink at their centers, with a rim of typical tumor cells at the edge. The marrow of the bone was replaced by a connective tissue reaction about the tumor cells. Several groups of mucous glands were seen toward the mucous membrane side of the tissue. Scattered bundles of skeletal muscle fibers were noted, as well as sheets of collagen fibrils.

The pathologist's diagnosis was squamous cell carcinoma.

The patient's progress was not particularly satisfactory. He was kept in the hospital until December 12, when he was discharged to his family physician for a daily change of the surgical dressings.

CASE 18—P. G., a Russian Jewish housewife aged 59, was admitted to the hospital June 13, 1929, with a provisional diagnosis of benign papilloma of the jaw. She was discharged as improved on June 20.

Her chief complaint was of a lump in the roof of the mouth. When she was 12 years old she had had a lump in the same location, which had been removed with a snare with the region under local anesthesia.

When she was 41 years old a piece of bone had been removed from the palate in an effort to check a beginning recurrence of the growth. She had been told that the granulation tissue about the wound would gradually shrivel of its own accord, which had occurred in about four years.

About nine months before admission the tumor had reappeared and had gradually increased in size. Most of the time the growth had been painless. Occasionally there had been a drawing sensation, and at other times it had ached, much as a tooth does. Formerly the growth had been rather soft and had seemed to have a pedicle. The last time it had been soft, but with a broader base. It had not bled.

She had had chickenpox at 14 years of age, but no other illnesses except confinements for childbirth. There was no history of injuries or operations except those enumerated on the jaw.

The catamenia had begun at 17 and had been very irregular, with cramps. After the first child was born there had been no more cramps, but the periods had been irregular. The menopause had occurred at 53. It had not been followed by any bleeding or discharge.

Her greatest weight before she was married had been 130 pounds (59 Kg). This had gradually increased during married life to 160 pounds (72.6 Kg). At

the time of admission to the hospital it was 155 pounds (70.3 Kg) She had purposely lost 5 pounds (2.3 Kg) by dieting for four weeks before entering the hospital

Her mother had died of kidney trouble Her father had died accidentally One brother had died at 18 from pleurisy

Her husband was living and well She had one son and one daughter living and well She had lost one son at the age of 7½ years from scarlet fever Another son had died at the age of 10 days from a congenital gastrointestinal deformity She had not had any miscarriages

General physical examination showed her to be well developed and slightly obese She appeared to be about 48 years old She was active mentally and physically Her hair was beginning to turn gray Her pupils reacted to light and in accommodation The pupils were equal and round The ocular movements were normal The ears and nose were grossly normal Many of the teeth had been extracted Those remaining were in poor condition Several teeth were carious, and there was pyorrhea

On the inferior surface of the hard palate, to the left of the midline, there was a growth about the size of the end of the little finger This growth had a distinct border and was lobulated on the surface It was fairly hard to palpation, but it gave the impression of fluid under tension rather than of stony hardness It was not painful and was adherent to the surrounding tissue Above the upper left canine tooth there was a scar where the piece of bone had been removed

The pharynx was somewhat injected, and the tonsils were atrophic There was no cervical adenopathy The thyroid was neither visible nor palpable The breasts were large and pendulous There were no masses The expansion was good and was equal on the two sides There were no abnormal percussion notes The voice sounds were normal There were no rales The heart sounds were slightly rapid but of good quality There were no murmurs The aortic second sound equaled the pulmonic The blood pressure was 170 systolic and 105 diastolic

The abdomen was large and fleshy There was no tenderness No abdominal masses were felt The vagina was short and the cervix fairly smooth On account of the thick abdomen a bimanual examination was impossible The impression was that there were some pelvic adhesions

Both legs were large and fleshy The left leg had many varicose veins, with increased pigmentation and an old scar from a broken-down varicosity

The diagnosis was mildly malignant tumor of the hard palate

On June 14 and 19 urinalysis gave negative results On the former date value for hemoglobin was 86 per cent by the Dare test, the erythrocytes numbered 5,810,000 and the leukocytes 8,400 per cubic millimeter, with polymorphonuclears 58 per cent, small lymphocytes 40 per cent and eosinophils 2 per cent

The radiologist on June 13 reported both antrums dull but the left more dense The region of the upper incisor teeth was less sharply defined than normal One left lateral incisor was missing

On June 19, with the region under local anesthesia induced by ¾ grain (0.01 Gm) of morphine sulfate and 1 grain (0.06 Gm) of cocaine hydrochloride U S P applied as paste with a solution of epinephrine hydrochloride 1:1,000 on an applicator, the granuloma was removed surgically from the lingual surface of the left superior alveolar process The small cavity exposed contained an aberrant tooth, and this was removed with a curet The bony cavity was curetted and found to be sound in every direction The wound was cauterized with the galvanocautery Sutures were not used

The postoperative clinical diagnosis was dentigerous cyst

The pathologist reported that the specimens consisted of two small pieces of soft tissue and a tooth. The soft tissue was dark red and rather hard from drying. The tooth measured 0.8 by 0.6 by 0.5 cm. Microscopic examination showed that the soft tissue was made of dense fibrous tissue. There was moderate vascularity. Around the edges of the section there were many polymorphonuclear leukocytes. There was some stratified squamous epithelium on one surface.

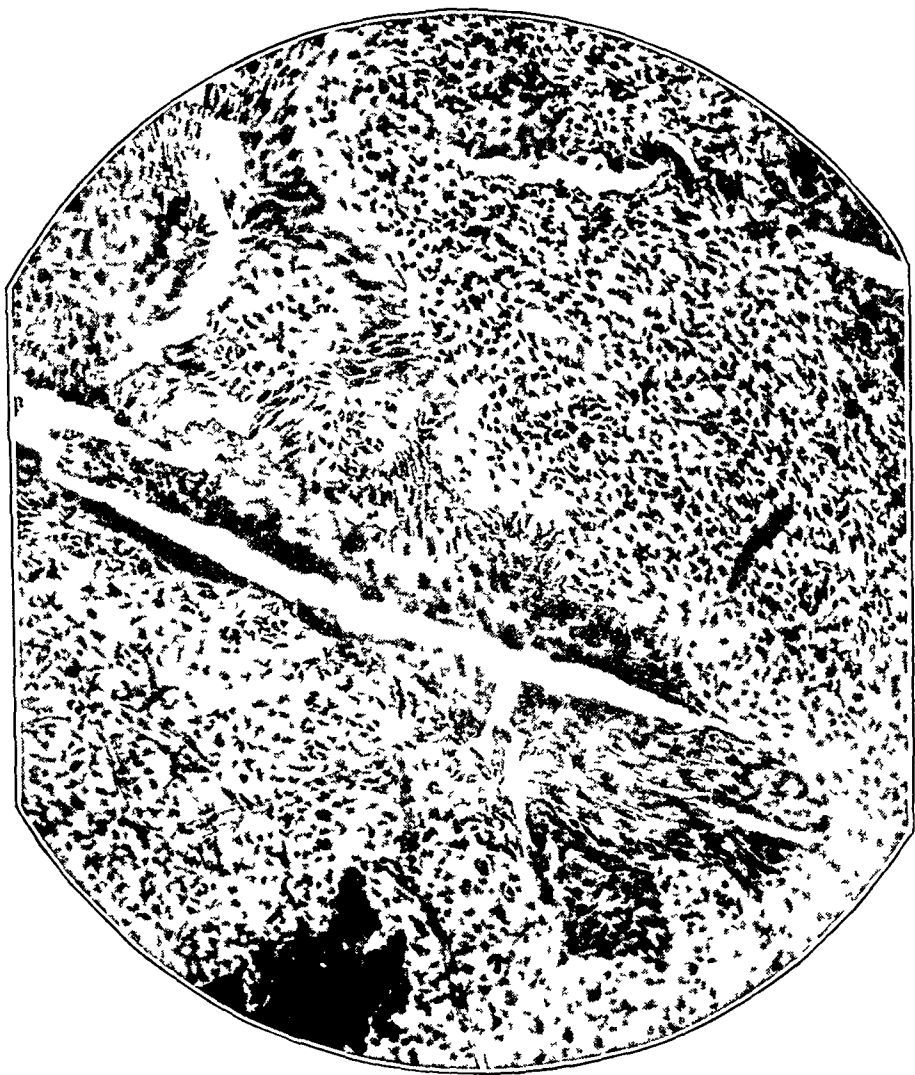


Fig 15 (case 18) —Photomicrograph of inflammatory tissue from a dentigerous cyst of the upper jaw

The pathologist's diagnosis was acute inflammation of the gingiva with scar tissue formation.

The patient was dismissed as improved on June 20.

CASE 19—J. D., an Irishman aged 49, a sheep herder, was first admitted to the Colorado General Hospital on Nov. 10, 1932, with a diagnosis of sublingual cyst.

His chief complaint was of a sore throat and tongue, worse on the left side.

His father had died of heart disease at 65. His mother was living and well at 80. He had two brothers and two sisters living and well. One brother had

died after an accident, and one had died from appendicitis. There was no family history of cancer, tuberculosis, diabetes, hemophilia or Bright's disease.

The patient had been born in Ireland and had come to this country at the age of 25. He had had measles in childhood. He had not had chickenpox, smallpox, scarlet fever, tuberculosis, pneumonia, rheumatic fever, gonorrhea or syphilis. He had had colds and sore throat infrequently. He had had a tonsillectomy at the age of 42, and his appendix and gallbladder had been removed at the age of 45. He had not had any injuries.

Three or four months before admission his throat and tongue had become sore. He had had headache once in a while, and there had been a roaring in his head, which started a month before the sore throat. The sore throat, sore tongue and roaring had persisted. This soreness had kept him from eating but had not interfered with talking and breathing. For a long time he had had nausea, vomiting and dizziness about once a month. He had thought that this was due to dietary indiscretions.

General physical examination showed that the head was normal. The pupils were of equal size and reacted to light and in accommodation. The ears were externally normal. The nose was normal. He was convalescing from a submucous resection of the nasal septum. Many of his teeth had been extracted, and he wore an upper plate. His gums were normal. His tongue was moist and had a heavy gray coat. It was very swollen and tender posteriorly. The floor of the mouth was very edematous. There was a small, semisoft nodule palpable beneath the tongue on the left side. The tonsils were enucleated. The pharynx was normal. The submaxillary lymph nodes were palpable on both sides. There was tenderness on deep pressure above the hyoid bone. There was no other adenopathy.

His chest was well developed but bony. It was resonant throughout. The breath sounds were vesicular. The tactile fremitus and vocal fremitus were normal. There were no rales. The pulse rate was 70, and the pulse was regular. The vessel wall was palpable. The heart was not enlarged or displaced. The sounds were regular, faint and distant. No shocks or thrills were felt. The pulmonary second sound was greater than the aortic. There were no murmurs. The blood pressure was 110 systolic and 70 diastolic.

The abdomen was flat and rigid. There was a long oblique scar in the right upper quadrant. There was no tenderness, and no masses could be felt. The genitalia were normal. The extremities were essentially normal. The reflexes were present and equal. There were no abnormal reflexes.

The diagnosis on admission was sublingual cyst.

The radiologist reported that there was no evidence of a salivary calculus.

Urinalysis gave negative results. The value for hemoglobin was 90 per cent by the Dare test. The erythrocytes numbered 4,750,000 and the leukocytes 10,300 per cubic millimeter, with polymorphonuclears 83 per cent, small lymphocytes 11 per cent, endothelial cells 3 per cent and eosinophils 3 per cent. The Wassermann reaction of the blood was negative.

On November 26 the dextrose content of the spinal fluid was 62 mg and the total protein content 45 mg per hundred cubic centimeters. The Wassermann reaction of the spinal fluid and the colloidal gold curve were both negative.

The ophthalmologist who saw the patient in consultation found the fundi normal, but he recommended bifocal lenses. The general surgeon who saw him believed a salivary calculus to be the most likely cause of the swelling. The dental consultant extracted the upper left first bicuspid on account of pyorrhea and a gold crown. The neurologist suspected Meniere's syndrome but found all the reflexes normal. The vestibular tests gave negative results.

The otolaryngologist, at the operation, made an incision in the floor of the mouth and in the base of the tongue on the left side. He used a needle to aspirate the mass for pus, but he could not find any pus. He was not able to explain the mass satisfactorily. However, the patient gradually improved subsequently, so that he was almost entirely well when he was discharged, on December 20.

SUMMARY AND CONCLUSIONS

Of the 19 cases reported, 15 were cases of malignant tumor and 4 of benign tumor. The social service agencies have been able to trace only 1 of the 19 patients. The Italian boy, who had fibrosarcoma over six years ago, is living and well. The 15 patients with malignant disease are probably all dead. The 4 with benign tumors should be living. One patient had a basal cell carcinoma on one side of the jaw and a squamous cell carcinoma on the other. All of the patients were admitted to the hospital for diagnosis and treatment at a late stage of the disease. All those with malignant tumors were made more comfortable and their lives prolonged by radium and roentgen therapy.

ROLE OF SULFANILAMIDE IN THE TREATMENT OF ACUTE OTITIS MEDIA

JAMES WOODS BABCOCK, M D

NEW YORK

The proper evaluation of a drug in therapy of a specific condition is often difficult. It is safe to assume that if a large number of remedies are recommended for one ailment it will heal spontaneously and that none of them have any special merit. It is also safe to assume that if a drug is outstandingly successful in the treatment of one or more diseases it will be tried on many others. This has been, and still is, the status of quinine, which, because it cured malaria, was asked to cure many ills for which it did no good. Arsphenamine held a similar role.

Sulfanilamide has produced such miraculous results in such a wide field that it is called on to do anything. Its value for certain diseases has sometimes been called into question.

In treatment of otitis media its value has been tested, and the reports have been controversial. I wish to report the findings of two members of my staff in Vanderbilt Clinic, Drs. E. B. Bilchick and G. H. O'Kane, who, one using sulfanilamide and the other not using it, observed 103 cases during the first three months of 1939.

METHOD

Fifty-five patients received sulfanilamide in doses such as are advised in the book by Long and Bliss¹ as moderate. The control group of 48 did not receive the drug. All the patients were children from 6 months to 10 years of age and were unselected. All received prompt myringotomies, none being treated by the drug alone. Only 6 patients showed any untoward effect of the medication, 4 having fever, 1 vomiting and 1 suffering from hallucinations. In both groups accompanying disease of the nose or throat was treated and the ears were treated by dry wipes or irrigations. Roentgenograms were taken if the discharge lasted over a week, and if mastoiditis seemed established the child was admitted to Babies Hospital and was followed there.

RESULTS

The observations made in the study are shown in the tables

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¹ Long, P. H., and Bliss, E. A. *The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds*, New York, The Macmillan Company, 1939.

Drs Bilchick and O'Kane and I have felt that on the whole the results in the two groups differed little. The average length of discharge was less by one third in the treated group. However, the percentage of the treated group requiring operation was higher than that of the control group. Earlier results in studies made in Babies Hospital² were reported as questionable, although all patients recovered, for the course that the disease would have followed if the drug had not been used could not be accurately predicted.

TABLE 1—*Bacteriologic Findings in Cases of Patients with Acute Otitis Media*

	In 55 Patients Treated with Sulfanilamide	In 48 Patients Not Treated with Sulfanilamide
<i>Streptococcus haemolyticus</i> beta	21	18
<i>Pneumococcus</i>	10	7*
<i>Staphylococcus aureus</i>	4	9
<i>Pfeiffer's bacillus</i>	2	
<i>Streptococcus viridans</i>	2	
<i>Staphylococcus albus</i>	9	10

* *Pneumococcus* type III was observed in 2 patients in the control series

TABLE 2—*Summary of Data on Both Groups*

	Patients Treated with Sulfanilamide		Patients Not Treated with Sulfanilamide	
Number	55		48	
Age	6 mo to 10 yr		5 mo to 11 yr	
Sex				
Male	24		26	
Female	31		22	
Number with unilateral otitis media	36		31	
Number with bilateral otitis media	19		17	
Total number of ears affected	74		65	
Number of myringotomies	35		43	
Total days of discharge after onset of treatment	387		600	
Average number of days of discharge after onset of treatment	8.6		12.6	
Total number of reactions	6			
Number admitted for operation	9 (16%)		5 (10%)	
Number on whom simple mastoidectomy was performed	6*			
Number operated on for revision of simple mastoidectomy	3		4†	
Number of complications	0		0	
Number of deaths	0		0	

* The organism in all the patients treated with sulfanilamide and coming to operation was *Str. haemolyticus* beta.

† The organisms in all the patients not treated with sulfanilamide and coming to operation were as follows: *Str. haemolyticus* beta 2, *Staphylococcus aureus* 1, *Staphylococcus albus* 1, 8.3%.

Fisher³ reported 66 patients requiring mastoidectomy in a group of 97 patients with otitis media who did not receive the drug, which seems to me a high percentage, and only 7 requiring operation in a group of 87 who were given sulfanilamide. There was no such contrast in our series.

2 McIntosh, R., Wilcox, D. A., and Wright, F. H. *J. Pediat.* 11: 167, 1937.

3 Fisher, G. E. *Sulfanilamide in the Treatment of Otitis Media*, *J. A. M. A.* 112: 2271 (June 3) 1939.

Cases have been reported ⁴ in which cortical perforations subsided without operation with the use of sulfanilamide alone. We had 3 analogous cases of abscesses forming under the scar of a previous mastoidotomy, in none of which was benefit received from the treatment with sulfanilamide.

There have been fewer cases of surgical mastoiditis during the past two years, in New York at least. However, a great difference in the incidence in different years was observed long before sulfanilamide was used.

Baker and Bradford ⁵ reported 11 cases of otitis media due to hemolytic streptococcus, 4 with signs suggestive of mastoiditis in which there was recovery without operation and 2 cases of otitis media due to Pneumococcus type III in which the ears were dry in four days and in which sulfanilamide was administered. We have recently been using sulfapyridine in preference to sulfanilamide in cases of the infections due to pneumococcus. Livingston ⁶ reported 5 cases of surgical mastoiditis in which sulfanilamide therapy was given and in which recovery occurred without operation.

This paper seems so far rather skeptical and pessimistic in contrast to some of the enthusiastic reports offered by others. This attitude should not be interpreted as indicating lack of appreciation of the all but miraculous wonders performed by sulfanilamide and its allied drugs in treatment of a large number of grave illnesses. In our field the results in cases of otitic meningitis are the most outstanding achievement. Anything that can reduce the mortality in this condition from 96.8 per cent to 35 per cent deserves the greatest respect and heartfelt thanks to its discoverers ⁷.

Maybaum, Snyder and Coleman ⁸ have well pointed out some of the dangers attendant on the use of sulfanilamide in treatment of otitis media, first, the danger of masking symptoms while a destructive process is going on as often occurs in cases of infection due to the pneumococcus type III, and he advised, as a test discontinuing the administration of the drug after using it a week, to see if symptoms recur. Smith and Coon ⁹ reported a case in which the patient seemed well

4 (a) Vaisberg, M. *Laryngoscope* **48** 54, 1938. (b) Long and Bliss ¹

5 Baker, D. C., Jr., and Bradford, G. E. *Sulfanilamide Therapy for Acute Otitis Media and Acute Mastoiditis*, *Arch Otolaryng* **29** 344 (Feb.) 1939.

6 Livingston, G. S. *Ann Otol, Rhin & Laryng* **46** 1127, 1937.

7 Neal, J. B., and Appelbaum, E. *Am J M Sc* **195** 175, 1938.

8 Maybaum, J. L., Snyder, E. R., and Coleman, L. L. *Experiences with Sulfanilamide Therapy for Otogenous Infections, with Special Reference to Masking of the Clinical Course*, *Arch Otolaryng* **30** 557 (Oct.) 1939.

9 Smith, H. B., and Coon, E. H. *Meningitis Due to a Hemolytic Streptococcus. Report of Two Cases with Recovery After the Use of Prontosil and Sulfanilamide*, *Arch Otolaryng* **26** 56 (July) 1937.

except for septic fever but actually had pus and streptococci in the cerebrospinal fluid and eventually recovered. A curious condition was found in 2 patients on whom mastoidotomy was performed at Presbyterian Hospital after use of sulfanilamide. Pus was present in a broken-down cavity, but the bone of the intercellular septums was brittle and no mucosa or granulations were present. The impression was that the bone was dead but not sequestered, as it felt like that of a cadaver. Another patient, after taking sulfanilamide for five weeks, showed many normal cells with groups containing pus and diseased bone scattered among them.

I shall not dwell on the cyanosis, rashes, vomiting and other well known occasional results of taking drugs of the sulfanilamide group. However, I should like to call attention to one occasional effect which may cause much needless worry. That is, elevation of temperature, which is particularly apt to occur in persons with hyperthyroidism. I have observed a case in which the temperature reached 106 F. before some one thought of discontinuing administration of the drug, after which it fell to normal in twenty-four hours. When a person taking sulfanilamide has unexplained fever, it is well to discontinue administration of the drug for at least twenty-four hours to see what effect is obtained. Hallucinations and mental excitement may also prove troublesome and are also more apt to occur in persons with hyperthyroidism.

CONCLUSION

I do not wish to give the impression that I do not appreciate the fact that sulfanilamide is a marvelous boon to mankind. It is true, however, that a number of my colleagues and I feel that its effect in the treatment of acute otitis media is somewhat overrated. This opinion may raise a storm of protest that should be instructive.

20 East Fifty-Third Street

SURGICAL TREATMENT AND ITS COMPLICATIONS IN CASES OF ACUTE SINUSITIS

W. LIKELY SIMPSON, M.D.

MEMPHIS, TENN.

Irrigation of the antrum through either the inferior or the middle meatus is probably done much more often than all other operative procedures on the nose. It seems to me that it is of no great importance whether the antrum is washed through the inferior or the middle meatus, but that of more importance is with how much care the irrigation is performed. Harm may be done by either approach, but if proper attention is given practically no complications from either method should be encountered.

If for any reason the antrum does not permit irrigation after puncture with only slight pressure, the procedure should be abandoned for at least twenty-four hours, when as a rule the normal irrigation can be made. The mucous membrane of the antrum may be edematous or polypoid, and in twenty-four hours this condition usually is corrected to such an extent that the irrigation can be carried out. I have never encountered any thing but good results from washing acutely diseased antrums which need drainage and see no good reason for not carrying out this procedure.

The anterior end of the middle turbinate is at times removed so that irrigations and suction of the frontal sinuses can be done. But I think that unless there is an acute infection of an ethmoid or a frontal sinus, which is threatening complications, this procedure is not indicated. The removal of a part or all of the anterior portion of the ethmoid bone gives sufficient approach to the frontal sinuses without the removal of the anterior end of the middle turbinate. Rarely the removal of the entire middle turbinate is indicated for drainage of an acute infection of a frontal or an ethmoid sinus, especially if complications are threatening.

SIMPLE ANTRUM OPERATION

The opening of the antrum in the inferior meatus is often done in cases of acute infection in this cavity. If the operation is carefully and completely performed it brings about an early end to such an infection. Many operators feel that this procedure is less painful and more

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satisfactory than irrigation of the antrum, especially for patients of a nervous type. A large opening with clean edges should be made, and trauma to the inferior turbinate avoided if possible.

Trauma to the inferior turbinate in little children is difficult to avoid at times, and some authors, especially Robb,¹ have suggested making an opening in the inferior meatus with a curved hemostat, and not attempting to obtain a permanent opening.

In cases of low grade infections of the antrum, with little pathologic change in the mucous membrane, the simple antrotomy is often all that is indicated, and the results in a high percentage of cases are satisfactory. A good opening in the inferior meatus gives aeration, even though it has been shown, as in the work of Hilding,² that drainage often does not take place through this opening. Irrigation of the antrum through a good opening in the inferior meatus even in small children is certainly a much simpler procedure than irrigation performed by means of a puncture in either meatus.

ACUTE SINUSITIS WITH COMPLICATIONS

Emphasis should be placed on the fact that drainage only should be sought in cases of acute and fulminating sinus infections. In ethmoid and frontal sinus infections with complications such as orbital abscesses, periostitis and osteomyelitis, external drainage should be obtained without any attempt to do a complete operation. If an external opening resulting in good drainage and without closure is made, the prognosis is much better than if an exenteration of the frontal or the ethmoid sinus is attempted. If a complete operation is indicated it should be done after all acute infection has subsided. Usually in one to two months this procedure would be safe.

Many a patient has lost his life because of too much surgical procedure at the time of the acute infection. It seems to me that intra-nasal surgical intervention in the presence of sinus complications such as periosteitis and orbital abscesses is not so good as external drainage, and that this is especially so in cases of little children.

ORBITAL COMPLICATIONS

The forms of orbital complications arising from acute sinusitis are somewhat varied, there may be, for instance, osteitis with or without necrosis, or even osteomyelitis, periosteitis, with or without subperiosteal abscess, or orbital infection of the soft tissue, which may be rather diffuse or at times may have rather a definite wall or capsule. Orbital

1 Robb. Personal communication to the author.

2 Hilding, A. Ciliary Activity and Course of Secretion Currents of Nose, Proc. Staff Meet. Mayo Clin. 6: 285-287, 1931.

abscesses outside the periosteum should be rare in such cases as come under a rhinologist's observation

Theisen,³ speaking of orbital complications in infants and young adults, stated, "The radical operation is imperative and prefers the external route" He said also, "The danger of the endo-nasal operation in children even in the hands of the most skillful operator is considerable"

Faulkner,⁴ in discussing Theisen's paper, said, "He cleans out the ethmoids which have ruptured into the orbit thoroughly as if he were doing a mastoid operation"

For the milder infections of the ethmoid sinus and the antrum, Porter⁵ advised the following procedure "particularly in children the removal of the anterior end of the middle turbinate and opening of the ethmoid labyrinth with possibly intranasal antrotomy, and in some cases of adults, it might be well to do a radical operation instead of the intranasal" If infiltration of the orbital tissue has already set in, he advised an external operation, with exenteration of the ethmoid sinuses and removal of the floor of the frontal sinuses, if the latter are diseased, as well as a Luc-Caldwell operation on the antrum

Coakley,⁶ in discussing Porter's paper, said, "In adult cases the intranasal operation is preferred, unless you have evident fluctuation"

Phelps,⁷ speaking of orbital cellulitis in children, said his method was to do an external operation with the patient under general anesthesia and break down the ethmoid bone, getting free drainage into the nose In his procedure, the antrum is opened from above in small children and in the inferior meatus in larger children, and the frontal and sphenoid sinuses are opened when such procedure is indicated Drains from the sinus are left in the nose, and the external incisions are almost entirely closed The drains are removed in twenty-four hours

Logan Turner,⁸ in discussing orbital complications arising from the anterior group of cells, said that "An external operation is usually necessary and that pus in the orbit should be evacuated at once to prevent loss of sight or intracranial complications"

3 Theisen, C F Ethmoiditis in Infants and in Young Children, with Accompanying Eye and Orbital Complications, *Arch Otolaryng* 8 386-398 (Oct) 1928

4 Faulkner, in discussion on Theisen³

5 Porter, C T The Etiology and Treatment of Orbital Infection, *Tr Am Laryng A* 53 123-135, 1931

6 Coakley, in discussion on Porter⁵

7 Phelps, K A Cellulitis of the Orbit in Infants and Children, with a Report of Ten Cases, *Tr Am Acad Ophth* 28 115-131, 1923

8 Turner, A L, and others Diseases of the Nose, Throat and Ear, ed 4, Baltimore, William Wood & Company, 1936, p 93

Hajek,⁹ writing of orbital complications resulting from suppuration in the sinuses, stated "In pronounced orbital affections the only principle which leads to good results is exposure of the diseased accessory sinus, by radical operation. Establishment of a wide communication with orbit, removal of all necrotic tissue and establishment of adequate drainage endonasally and extranasally."

In closing this discussion of orbital complications arising from an accessory sinus infection, I should like to mention some of the operative procedures which have become somewhat routine in my work and which have been helpful to me. First I would mention that intranasal operation on infants and little children with orbital complications of the ethmoid sinuses seems to me unsatisfactory and more dangerous than operation by the external route, while the intranasal opening of the antrum is easily done.

It appears to me that in all cases of orbital complications resulting from accessory sinus suppuration the external route is the more satisfactory. Any operative procedure which is necessary can be done accurately and thoroughly by the external approach. In the cases in which the infection is acute no attempt is made to do a thorough removal of all the septums as mentioned by Faulkner. If the affected sinuses, frontal, ethmoid or others, are widely opened and a drainage tube is inserted without the wound's being closed the prognosis is much better than if a complete radical sinus operation is done. Any necessary operative procedure on the sinuses can much more safely be carried out after the acute infection has subsided. If there is a fistula and the condition is less acute, more complete surgical work on the affected sinus is often indicated. In my work a complete radical operation on the frontal sinus or the antrum in the case of an acute sinus infection with an orbital complication is not done, only drainage of the affected sinus and the orbital suppuration is attempted at the primary operation, the thorough surgical procedure being left until the acute infection has subsided. It seems to me that much unnecessary risk is taken when a radical surgical procedure is done in these cases of acute infection. Many of these sinuses, when little if any infection was present before the complicating attack, go back to normal without further operative procedure, but of course if there was an old chronic infection previous to the attack it is necessary to do a radical operation later to bring about a good result.

If one has an opportunity to observe these cases of orbital complication it is seldom necessary to open an abscess outside the periosteum of the orbit, as in practically all such cases drainage would have occurred

⁹ Hajek, M. Pathology and Treatment of the Inflammatory Diseases of the Nasal Accessory Sinuses, translated by J. D. Heitger and F. Hansel, St. Louis, C. V. Mosby Company, 1926, vol. 2, p. 602.

at least by the time a subperiosteal abscess had formed. If there is an abscess in the orbit outside the periosteum it should be drained through the periosteum, through an external wound or through a skin incision.

Closure of the wound, especially in cases of acute infection, has not been done in my cases, and good cosmetic results are practically always obtained. A secondary closure is usually unnecessary.

OSTEOMYELITIS OF BONES OF THE FACE AND SKULL

Osteomyelitis of facial bones, resulting from suppuration of the antrum and the ethmoid sinuses, seldom becomes progressive and destructive, as osteomyelitis of the frontal bone, resulting from diseases of the frontal sinus, is seen to do only too often, since there is no frontal sinus in infants and very small children they seldom, if ever, have such a condition. Osteomyelitis of the ethmoid bones and of the superior maxillary, lacrimal and nasal bones is not uncommon. A more conservative operative approach is indicated in cases of osteomyelitis of the face than in those of fulminating, progressive infection of the frontal bone.

OSTEOMYELITIS OF THE SKULL

Osteomyelitis of the skull as a complication of infection in the frontal and other sinuses is somewhat different from osteomyelitis of the facial bones caused by such infection. There is only rarely osteomyelitis of the skull resulting from infection in the antrum or the ethmoid sinuses, and only slightly more often, from infection in the sphenoid.

Practically all of the osteomyelitis which I see is caused by acute sinus infection or by acute exacerbation of a chronic sinus disease. I have seen only one osteomyelitic infection coincidental with an operative procedure on a frontal sinus. This was in a case of moderately acute pansinusitis, in which a Lynch type of operation was done, before this operative procedure there was probably a low grade osteomyelitis which was not recognized at the time of the operation, for the osteomyelitic symptom appeared immediately after the opening of the frontal sinus. Some writers say that most of the osteomyelitis of the skull results from operative procedures on the frontal sinus, but in the hospital of the University of Tennessee and in my private work my fellow-workers and I see practically no osteomyelitis as a complication of surgical intervention performed on the frontal sinus. If only drainage is done in cases of acute sinusitis, with as little trauma as possible to the bones of the face and frontal region, little osteomyelitis should occur. Of course, it is understood that sufficient drainage of the correct type and at the opportune time should be carried out.

Practically all rhinologists agree with the plan of attack on osteomyelitis of the skull as outlined by Mosher,¹⁰ Furstenburg¹¹ and others, that is, that all diseased bone should be thoroughly removed and that a moderate amount of the normal surrounding bone should be removed also. There is usually edema of the soft parts over the bone in a wider area than the roentgenogram indicates, and the extent of this edema is a more accurate gage of the disease in the bone than the roentgenogram is. I believe a word of caution, however, is not out of order, and that is that all swelling and edema of the frontal region is not osteomyelitis. Often one may see edema of the frontal region in the absence of osteomyelitis, but when a positive finding is obtained by means of the roentgenogram or otherwise the extent of the edema is indicative of the extent of the osteomyelitis.

It seems to me well to say also at this time that in most cases osseous necrosis and cranial osteomyelitis are not progressive, fulminating osteomyelitis of the skull and that they require only local drainage and moderate removal of necrotic osteomyelitic bone. The surgeon must be alert, however, and recognize that temporizing with the fulminating, progressive type of osteomyelitis will end only in complications, such as brain abscess, meningitis and sinus thrombosis.

10 Mosher, H. P. Osteomyelitis of Frontal Bone. Notes on Three Cases, *J. A. M. A.* **107** 942-947 (Sept. 19) 1936.

11 Furstenburg, A. C. Osteomyelitis of Skull. Osteogenetic Process in Repair of Cranial Defects, *Tr. Am. Laryng., Rhin. & Otol. Soc.* **37** 1-18, 1931.

INTRADURAL CONDITIONS IN RELATION TO RHINOLOGY AND OTOTOLOGY

CRITICAL SURVEY OF RECENT LITERATURE

WELLS P EAGLETON, MD

NEWARK, N J

(Concluded from page 120)

TREATMENT OF MENINGITIS

EXPERIMENTAL WORK ON THE CURE OF MENINGITIS

Experiments with Horse Serum—Burtenshaw¹³⁴ attempted to ascertain what proportion of the serum which had been administered parenterally to patients suffering from meningococcic meningitis in reality reached the cerebrospinal fluid

Antitoxin Precipitin Reaction For this purpose he used an adaptation of the precipitin reaction for the presence of antitoxin-containing horse serum in the body fluids Twenty-three patients with meningococcic meningitis and 1 patient from whom only a strain of staphylococcus could be isolated were used Each received meningococcus antitoxin by intravenous injection Horse serum protein was detected in the cerebrospinal fluid in every case, though its concentration varied greatly and was always small compared with that in the blood

Burtenshaw stated (1) that intrameningeal injections of serum insure the immediate presence of large amounts of antibody at the site of infection, and yet (2) that the steepness of the drop in serum concentration following the injection is striking, for within one or two days the serum content of the cerebrospinal fluid has fallen to the low levels attained by parenteral administration alone, no matter how large the dose

Experimental Data on Efficiency of Forced Drainage in Inflammations of Cerebrospinal Fluid—The following observations were made by Riser and Planques¹³⁵ concerning the efficiency of forced drainage in dogs, effected by intravenous injections of a 0.35 per cent solution of sodium chloride after suboccipital puncture

134 Burtenshaw, J M L Detection of Horse-Serum (Meningococcus Antitoxin) in Blood and Cerebro-Spinal Fluid, *Lancet* **2** 1513-1516 (Dec 31) 1938, abstracted, *J A M A* **112** 1111 (March 18) 1939

135 Riser and Planques Drainage simple et drainage force du liquide cephalo-rachidien (Experimentation et applications cliniques), *Ann de med* **40** 317-353 (Nov) 1936, abstracted, *Arch Neurol & Psychiat* **39** 1326-1327 (June) 1938

1 Soon after the beginning of the continuous injections the flow of the spinal fluid was doubled and trebled 2 A constant stream of cerebrospinal fluid could be maintained for hours and even for days 3 The albumin and the cellular content of the fluid gradually increased, without change in the chlorides 4 The blood pressure gradually diminished, reaching a minimum after about two hours, and gradually returned to normal 5 Injections of a theobromine preparation caused an increase in the flow of cerebrospinal fluid parallel to the diuretic effect 6 This caused the amount of cerebrospinal fluid to diminish toward the end of the first hour, but after the third hour, with the appearance of diuresis, it returned to the level observed prior to injection of the solution of sodium chloride

Histologic examination of the brains and spinal cords of the dogs showed an increase in lymphocytes within the arachnoid meshes, which explains the mild increase in lymphocytes in the spinal fluid following forced drainage There was, however, no active cellular proliferation in the perivascular spaces of the brain or the spinal cord

These authors concluded that it is still too early to state definitely whether the method of forced drainage has a curative effect in different forms of meningoencephalitis, dementia paralytica and disseminated sclerosis For, although a considerable amount of cerebrospinal fluid is eliminated and the monocytes and albumin are increased these phenomena are merely signs of the reactions of the choroid plexus and the meningeal vessels They do not indicate drainage of the neural parenchyma itself

Comment by Reviewer It is my experience that forced drainage is extremely valuable in cases of meningitis in which no focus of primary infection is demonstrable at the beginning of treatment—that is, cases of meningitis associated with extensive skull fracture or of streptococcic meningitis occurring as the result of scarlet fever angina But it is of little value with the ordinary forms of otitic and rhinogenic meningitis and is debilitating These conditions require removal of the focus, repeated lumbar punctures and blood transfusions—W P E

TREATMENT OF MENINGITIS WITHOUT SULFANILAMIDE

Good Results of Early Operation in the Recovery of Meningitis—

In 1926 and again in 1931, Watson-Williams¹³⁶ published a series of 12 cases of meningitis, with 8 recoveries, of the 12 patients, 5 who were treated before the end of the second day from the onset of meningitis recovered while only 3 of the 7 treated on the third day or later got well In 1936, he recorded, "seven patients treated in less than three days from the beginning of the disease, all recovered"

¹³⁶ Watson-Williams, E Chemotherapy of Meningitis, *Lancet* **1** 807-808 (April 2) 1938

An Insufflation in the Treatment of Otitic Meningitis—Wasowski¹³⁷ reported 3 cases of suppurative meningitis in which the patients were treated by means of intraspinal insufflation of air, 2 of them recovered

One patient, who had meningitis from suppurative otitis, with cholesteatoma, recovered after repeated insufflations of air following a mastoid operation. In Wasowski's second successful case the meningitis supervened after operation for chronic suppuration of the middle ear.

Treatment by repeated air insufflation of the arachnoid space with air, which has been long in use in cases of epidemic cerebrospinal meningitis and tuberculous meningitis, was recommended by Brunder¹³⁸. He stated that adhesions can possibly be prevented by the procedure. Such adhesions often cause increased pressure by confining the pus in pockets.

Technic The cerebrospinal fluid is drained by lumbar puncture with the patient in the seated position, and 10 cc less of air than the amount of drained fluid is insufflated.

RESUME OF MY PRESENT VIEWS ON CURABLE MENINGITIS

Before the advent of sulfanilamide and its derivatives I collected from the literature over 150 cases of cured meningitis with bacteria free in the cerebrospinal fluid. Study of these cases taught certain facts that may help to explain why patients are cured today when treated with sulfanilamide and also why certain of them suffer a relapse. Before sulfanilamide was available I cured 27 patients¹³⁹ with meningitis associated with bacteria in the spinal fluid. My percentage of recoveries was 32 per cent in all my operative cases, but many patients did not have germs free in the fluid¹⁴⁰.

From an attempt to analyze the factors in the cases of these patients with bacteria free in the fluid who recovered I drew the following deductions:

As with all forms of suppuration, fixation of the infection is the most important factor favoring recovery. In meningitis this localization of (a) infected fluid or of (b) a small collection of free pus is apt to occur in an area of the pia-arachnoid adjacent to the diseased area in the

137 Wasowski, T. Ueber die Behandlung der otogenen eitrigen Hirnhaut-entzündung mittels intraspinaler Luftzuführung, *Monatschr f Ohrenh* **71** 557-561 (May) 1937.

138 Brunder, H. Neuere Wege in der Diagnose und Behandlung der otogenen Meningitis, *Wien med Wchnschr* **87** 840-846 (Aug 7) 1937.

139 Eagleton, W. P. Curable Cases of Meningitis, *Laryngoscope* **48** 150 (Feb) 1938.

140 Eagleton, W. P. Suppuration Meningitis of Otitic and Nasal Origin, *Arch Otolaryng* **15** 885-905 (June) 1932.

bone Thus, cure was brought about by (1) removal of the primary focus of infection, whether in the bone or in a vessel of the bone of the adjacent sinus, (2) drainage of the infected fluid or of an abscess of the pia-arachnoid and (3) the fact that the bacteria in the spinal fluid were (a) attenuated, (b) of low grade virulence or (c) few Additional and contributing factors were (4) that infection had lasted a sufficient time to allow a protective meningitis to develop and (5) that the sugar content of the cerebrospinal fluid was found to have continued, although the patients often were acutely ill

I am persuaded that the curative effect of sulfanilamide is due to a combination of the third and fifth factors and that the drug acts on the bacteria themselves, so interfering with their metabolism that they cannot propagate—they become attenuated at the same time by raising the electromotive force of the milieu, whether it be that of the cerebrospinal fluid or that of the pia-archnoid tissues Both actions are accomplished by an intermediate product during the process of oxygen reduction (E^h) that sulfanilamide causes when it comes in contact with freshly liberated oxygen

Several of my cured patients had the specific self-limited type of meningeal inflammation, which I have named (a) toxemic meningitis and (b) allergic overflow meningitis from scarlet fever or pneumonia ¹⁴¹

NONSURGICAL TYPES OF STREPTOCOCCIC AND PNEUMOCOCCIC MENINGITIS

These conditions should be regarded and treated differently from the usual localized meningitis of otitic or nasal origin ¹⁴² These two nonsurgical and non-tissue-destructive types of bacterial meningitis I would designate as

1 Toxemic scarlatinal meningitis, with an overflow of attenuated streptococci in the meninges

2 Pneumococcic toxemic overflow meningitis Both types frequently exhibit allergic phenomena The cerebral symptoms are apt to be due to anoxemia of the cerebral cortex The latter condition runs a self-limited course and may end by crisis Consequently, although any concomitant otitis media has to be attacked surgically, the meningitis itself should be regarded from the viewpoint of the self-limited nature of the causative scarlet fever or pneumonia

Furthermore, when the bacteria in the overflow are attenuated, the patient does not require cerebrospinal fluid drainage of any kind

¹⁴¹ Eagleton, W P, in discussion on Cuning, D S Treatment of Otitic Meningitis, Arch Otolaryng 30 950-972 (Dec) 1939, in discussion on Converse, J M Recurrence of Otitic Infections Due to Beta-Hemolytic Streptococcus Following Inadequate Sulfanilamide Therapy, Tr Sect Laryng, Otol & Rhin, A M A, 1939, pp 145-146, J A M A 113 1383-1387 (Oct 7) 1939

¹⁴² Eagleton, W P, in discussion on Symposium What Is Justifiable to Do in Otitic Meningitis? Tr Am Otol Soc 28 73-76, 1938

"Both of these types of nonsurgical overflow meningitis should be recognized as distinct entities"

NORMAL BRAIN METABOLISM

In both of these communications I suggested that the presence of sugar in the cerebrospinal fluid signifies that the normal metabolic action of the brain has not been interfered with, that in such a condition, although the meninges are the seat of a bacterial infection, the inflammatory process is not overpowering and can be controlled by the normal protective reactions of the meninx, and that this possibility is present as the metabolic action of the central mechanism continues

This is what takes place from the use of sulfanilamide. The drug acts in a similar way, by causing bacteriostasis and thus preventing the bacteria from paralyzing the metabolic mechanism of the brain

The explanation of relapses after the use of sulfanilamide is to be found in the fact that the drug has a bacteriostatic action only on the bacteria that it can reach. Sulfanilamide, even in high concentration in the blood or in the cerebrospinal fluid, does not act in the presence of encapsulated and necrotic tissue, for it cannot oxidize in a localized area of infection. It cannot reach and attack bacteria in areas of necrotic tissue

An illustration of this point is one of my cases of abscess of the brain, in which the patient, a child, apparently suffered from meningitis. A ventriculogram revealed the abscess in the occipital lobe. The abscess was opened, and the pus was full of streptococci, yet the cerebrospinal fluid had been free from microorganisms for many weeks, during which time the child had been given sulfanilamide continuously. There were hemolytic streptococci present in the abscess of the brain after sulfanilamide had sterilized the cerebrospinal fluid

EXPLANATION OF RECOVERIES FROM INFECTION AFTER USE OF SULFANILAMIDE AND INADEQUATE SURGICAL TREATMENT

USE OF SULFANILAMIDE IN CASES OF RECURRENT SYMPTOMS

In those cases in which sulfanilamide or one of its derivatives lowers the temperature and causes the disappearance of symptoms but the symptoms recur after a short interval, no further reliance should be placed on exclusive use of the drug. Furthermore, any possible infective focus should be drained or, if possible, eradicated. For within the purulent focus—be it in the bone or in the cerebral substance¹⁴³—there frequently are active organisms which because of the localization of the suppurative process cannot be affected by the circulating blood but which still possess invasive and toxic powers

¹⁴³ Eagleton,²⁴ case 7, p. 35

Cleary¹⁴⁴ concluded his thesis with certain principles which may well serve as a guide in the management of meningitis. They are

The operation of choice (in otitic meningitis) is the Eagleton operation, with wide exposure of the dura, and evacuation of the fluid of the basal cistern.

Continuous drainage is to be condemned.

If involvement of the petrous apex is suspected, it should be explored at the original operation.

The petrous apex is not infrequently a secondary focus.

In pneumococcic meningitis, the sphenoid sinus is to be suspected as a focus.

In pneumococcic meningitis specific serum whenever possible should be combined with sulfanilamide.

Repeated lumbar taps, small transfusions and general supportive treatment are important.

An unfavorable postoperative course may be due to a secondary focus in the opposite ear, or the petrous apex, in pneumococcic meningitis, it may be due to a focus in the sphenoid sinus.

The sugar content and the cytologic picture of a sterile cerebrospinal fluid are of great importance in prognosis, the differential count is of more significance than the total number of cells and may surpass the sugar content in importance.

An unfavorable postoperative course may be due to a secondary focus in the opposite ear or in the apex of the petrous pyramid, in cases of pneumococcic meningitis it may be due to a focus in the sphenoid sinus.

Sulfanilamide is a most valuable therapeutic agent for streptococcic and pneumococcic meningitis. It is nevertheless a toxic drug and should not be used without definite indications.

Patients given sulfanilamide in effective doses all showed cyanosis, due presumably to methemoglobinemia, as it disappeared promptly after reduction of the dose or withdrawal of the drug. The only other toxic effect observed was diarrhea in 2 patients, 1 of whom had bloody stools. In case 7 there was a history of disease of the gallbladder and slight jaundice on admission. In other cases I have seen vomiting but none of the rest of the toxic symptoms mentioned in the literature. Administration of the drug is thus better maintained. In doses considered adequate, the blood concentration ranged from 9 to 13 mg per hundred cubic centimeters. In other patients given large doses of "prontosil" Cleary has seen a bright pink blush of the entire skin, which was not a dermatitis but appeared to represent a concentration of the drug in the skin itself.

CHEMOTHERAPY FOR MENINGITIS

The introduction of the sulfonamide derivatives as bacterial chemotherapeutic agents in the treatment of suppuration of the meninges is

144 Cleary, J. A. Thesis, University of Pennsylvania Graduate Medical School, 1938, Cranio-Otological Service, Newark, N. J., Eye and Ear Infirmary.

to be regarded as the "greatest stride in therapeutics that has occurred in recent years, comparable only to the results from the organic arsenicals" in the treatment of syphilis obtained by Ehrlich (Heathcote)

PHARMACOLOGY OF THE AZO DYES AND SULFONAMIDES

The chemical structure of the sulfonamides and their specific therapeutic action on bacteria and the lower forms of life were described by Heathcote ¹⁴⁵

He said that "the term sulphonamides" requires some explanation ¹⁴⁵ "An amide may be regarded as the result of the substitution of the hydroxyl group of an organic acid by the amide group $-\text{NH}_2$." For example, substitution of the OH in acetic acid ($\text{CH}_3\text{CO OH}$) by $-\text{NH}_2$ yields acetamide, $\text{CH}_3\text{CO NH}_2$

"Similarly, a sulfonamide may be regarded as the result of replacement of the hydroxyl group of a sulfonic acid ¹⁴⁶ by the amide group, $-\text{NH}_2$ " (Heathcote)

Benzenesulfonamide, whose symbol is $\text{C}_6\text{H}_5\text{SO}_2\text{NH}_2$, is formed by the substitution of the amide group, $-\text{NH}_2$, in place of the hydroxyl group (OH) of benzenesulfonic acid, $\text{C}_6\text{H}_5\text{SO}_2\text{OH}$

Sulfonated organic compounds are more soluble but of less toxicity than the parent substance. In therapeutic pharmacology the general effect of the sulfonation of a simple organic compound is to produce a substance of (a) greater solubility in water but of (b) less toxicity and of (c) lower therapeutic value

Thus, phenolsulfonic acid (sulfocarboic acid), $\text{C}_6\text{H}_5\begin{smallmatrix} \text{OH} \\ \text{SO}_2\text{H} \end{smallmatrix}$, is less irritant and less toxic than the parent substance, phenol, $\text{C}_6\text{H}_5\text{OH}$. It is also much less powerful as an antiseptic, although much more soluble in water

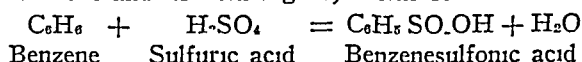
THE EARLY SULFONATED DYES

Several of the earlier chemotherapeutic agents, e. g., trypan blue, trypan red and germanin, first extensively used against trypanosomiasis ("the borers"), belong to the group of sulfonated dyes

¹⁴⁵ Heathcote, H. St. A. Sulphonamide and the Chemotherapy of Bacterial Invasion in Tidy, H. L., and Short, A. R. International Medical Annual, Baltimore, William Wood & Company, 1938, p. 465

¹⁴⁶ A sulfonic acid is a compound of SO_2OH with another radical

Sulfuric acid ($\text{H}\cdot\text{SO}_4$) acting as a hydrolytic agent on a variety of hydrocarbons (such as benzene and its homologues) forms sulfonic acids



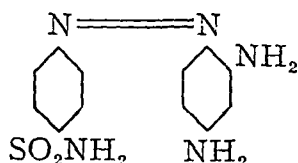
Thus, "a sulfonic acid results from the replacement of a hydrogen atom, directly linked to a carbon, in an organic compound by the group $-\text{SO}_2\text{OH}$ " (or $-\text{SO}_2\text{H}$)

However, until the introduction of the original prontosil (the hydrochloride of 4-sulfamido-2',4'-diaminoazobenzene), chloramine¹⁴⁷ was the only member of the sulfonamides that obtained wide application in medicine

Historical Background of Sulfanilamide and Its Derivatives—In 1908, Gelmo¹⁴⁸ synthesized paraaminobenzenesulfonamide. Heidelberger and Jacobs¹⁴⁹ pointed out that there was a certain chemotherapeutic effect from molecules containing the azo ($-\text{N}=\text{N}-$) coupling, for example, paraaminobenzenesulfonamideazohydrocupreine.

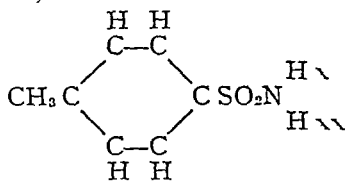
In 1920 the basic form of the original prontosil (4-sulfamido-2',4'-diaminoazobenzene) was patented in England. In 1932 a patent was obtained in Germany for the sulfonamide-containing azo dyes, also covering the hydrochloride of 4-sulfamido-2',4'-diaminoazobenzene (the original prontosil), which was used by Domagk¹⁵⁰ in his experiments. Whether it was Heidelberger and Jacobs'¹⁴⁹ observation of the effect of the azo coupling or pure chance that later led to Domagk's¹⁵⁰ experiments, in 1935 in the cure of an otherwise fatal streptococcal infection in mice is not known.

This compound was put out under the trade names of prontosil and prontosil flavum and others. It was a hydrochloride of 4-sulfamido-2',4'-diaminoazobenzene, the structural formula for which is as follows:

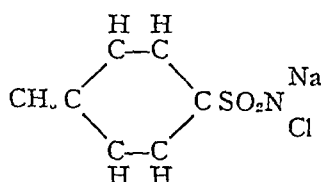


It is now abandoned.

147 Chloramine is derived from paratoluenesulfonamide by the replacement of two hydrogen atoms in the amide group by an atom each of sodium and chlorine (Heathcote).



Paratoluenesulfonamide



Chloramine

The hydrogen atom (H) marked v is replaced by a sodium atom (Na) and the hydrogen atom (H) marked v is replaced by a chlorine atom (Cl).

148 Gelmo, P. J. Prakt. Chem. **77** 369, 1908, cited by Long, and Bliss¹⁶⁴

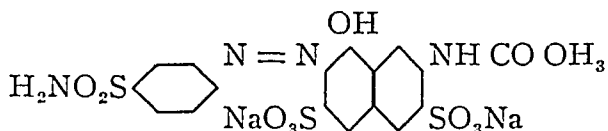
149 Heidelberger, M., and Jacobs, W. A. Synthesis in the Cinchona Series. III. Azo Dyes Derived from Hydrocupreine and Hydrocupreidine, J. Am. Chem. Soc. **41** 2131, 1919.

150 Domagk, G. Ein Beitrag zur Chemotherapie der bakteriellen Infektionen, Deutsche med. Wchnschr. **61** 250-253 (Feb. 15) 1935.

Later there appeared a more soluble compound (the sodium salt of 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3', 6'-disulfonic acid), called originally prontosil soluble

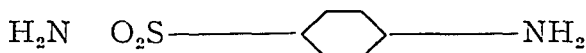
It was used in Domagk's further experimental and clinical observations Clinically Schreus found it highly effective

This compound was later called prontosil, and still later neoprontosil¹⁵¹ It is now known commercially as neoprontosil and has recently been given the nonproprietary name azosulfamide by the Council on Pharmacy and Chemistry of the American Medical Association Its graphic formula is as follows¹⁴⁵

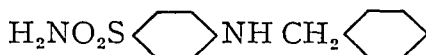


This compound could be given by intramuscular injection¹⁵³

Trefouel, Trefouel, Nitti and Bovet¹⁵⁴ (1935) found that a number of azo dyes prepared from paraaminobenzenesulfonamide (sulfanilamide) had an antistreptococcic action like that of "prontosil" (form not stated) They proposed the hypothesis that all the active azo dyes are reduced in the organism to paraaminobenzenesulfonamide (sulfanilamide) This led to the very important discovery that the azo linkage is unnecessary and that the simple colorless compound sulfanilamide is itself highly active as a therapeutic agent for experimental streptococcic infections The structural formula for sulfanilamide (which has been given the trade names prontylin and prontosil album and others) is as follows¹⁴⁵



A later benzylsulfanilamide is "proseptasine," or "septazine" (N⁴-benzylsulfanilamide) It is parabenzyaminobenzenesulfonamide Its structural formula is as follows¹⁴⁵



151 Lockwood, S J, Coburn, A F, and Stokinger, H E Studies on the Mechanism of the Action of Sulfanilamide I Bearing of the Character of the Lesion on the Effectiveness of Drug, J A M A **111** 2259-2264 (Dec 17) 1938

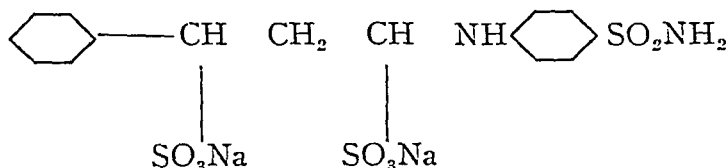
152 Footnote deleted

153 Schreus, H T Chemotherapie des Erysipels und anderer Infektionen mit Prontosil, Deutsche med Wchnschr **61** 255-256 (Feb 15) 1935

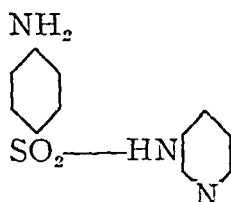
154 Trefouel, J, Trefouel, J (Mme), Nitti, F, and Bovet, D Activite du p-aminophenylsulfamide sur les infections streptococciques experimentales de la souris et du lapin, Compt rend Soc de biol **120** 756-758, 1935

155 Footnote deleted

Another derivative is soluseptasine (disodium p-[γ -phenylpropyl-amino]-benzenesulfonamide), which has the following structural formula ¹⁵⁶



The latest and now most popular sulfonamide compound is "sulfapyridine," called also by the trade names M & B 693 and dagenan. It is a derivative of sulfanilamide and is 2-(paraaminobenzene-sulfonamido)-pyridine, having the following structural formula



It differs from sulfanilamide in that one hydrogen atom of the SO_2NH_2 group is replaced by a basic pyridine group

Sulfapyridine has been advocated by Whitby ¹⁵⁷ as particularly active against pneumococci, exerting a definite action on the capsules of type I and type III pneumococci ¹⁵⁸. It is as effective, dose for dose, as sulfanilamide against hemolytic streptococci, having the advantage of being relatively nontoxic and yet active in relatively small doses

ACTION OF SULFANILAMIDE AND ITS DERIVATIVES

DIFFUSIBILITY OF SULFANILAMIDE COMPOUNDS

Sulfanilamide and its derivative sulfapyridine diffuse readily to all normal tissue and fluids of the body, thus resembling urea [$\text{CO}(\text{NH}_2)_2$] and ethyl alcohol ($\text{C}_2\text{H}_5\text{OH}$) in their equal distribution. The sulfanilamides readily pass into the cerebrospinal fluid ¹⁵⁹

¹⁵⁶ Beaumont and Dodds,¹²⁴ p. 3

¹⁵⁷ Whitby, L. E. H. *Chemotherapy of Pneumococcal and Other Infections*, with 2-(p-Aminobenzenesulphonamide) Pyridine, *Lancet* **1** 1210-1212 (May 28) 1938

¹⁵⁸ Telling, M., and Oliver, W. A. *Case of Massive Pneumonia, Type III, with Massive Collapse, Treated with 2-p-Aminobenzenesulphonamide) Pyridine*, *Lancet* **1** 1391-1393 (June 18) 1938

¹⁵⁹ Marshall, E. K. *Bacterial Chemotherapy. The Pharmacology of Sulfanilamide*, *Physiol. Rev.* **19** 240-269 (April) 1939. Marshall, E. K., Jr., Emerson, K., Jr., and Cutting, W. C. *The Distribution of Sulfanilamide in the Organism*, *J. Pharmacol. & Exper. Therap.* **61** 196-204 (Oct.) 1937. *Para-Aminobenzenesulfonamide. Absorption and Excretion, Method of Determination in Urine and Blood*, *J. A. M. A.* **108** 953-957 (March 20) 1937

SULFAPYRIDINE IN THE FLUIDS

Since there is no meningeal barrier for this molecule, almost the same level is found in the cerebrospinal fluid and in the blood. The product has been found in the nasal mucosa and aqueous humor (of the dog). The passage into the blood and spinal fluid is more rapid by several hours when the substance is injected by the intramuscular and intravenous routes.

Durel, Halpern, Dubost and Allinne¹⁶⁰ observed that sulfapyridine circulates not in the form of paraaminobenzenesulfonamide but in that of the pyridine molecule, i. e., in a chemical state peculiar to itself. It is found either in the state of free amine or in that of conjugate amine (acetyl derivative or glycuronic derivative in the urine).

ACTION OF SULFAPYRIDINE IN INFECTION

Whitby¹⁵⁷ and Telling and Oliver¹⁵⁸ suggested that sulfapyridine exerts a direct action on the capsules of the type I and the type III pneumococcus. Sulfapyridine therapy, according to the observations of Hilles and Schmidt,¹⁶¹ leads to the production of decapsulated pneumococci. However, there is no indication whether this is the result of capsular degeneration or inhibition of capsule formation. Avirulent decapsulated type XXII pneumococci have been isolated from the blood of mice treated with this drug.

Experiments have shown that sulfapyridine has a curative action when administered to mice infected with pneumococci of types I, IV, V, VI A and VI B, VII, XI, XX, XXII, XXIV, XXVII and XXIX. The drug has little curative action for infections with type II, III and VIII pneumococci (Hilles and Schmidt).

COMPARATIVE EFFECTS OF SULFAPYRIDINE AND SULFANILAMIDE IN TYPE II PNEUMOCOCCIC INFECTION IN MICE

Raiziss and his co-workers¹⁶² found that, while sulfapyridine is somewhat more potent than sulfanilamide in the treatment of type II pneumococcic infection in mice, it does not cure the infection but prolongs the animals' life. The superiority of sulfapyridine over sulfanilamide is only in the delay of death by two days.

160 Durel, P., Halpern, B. N., Dubost, P., and Allinne, M. Passage dans le sang, dans le liquide céphalo-rachidien et dans les urines de l'a (*p*-amino-phényl-sulfamido) pyridine [693], *Presse med* **47** 920-924 (June 10) 1939, abstracted, Neuro-Psychiatric Institute of the Hartford Retreat, series 7, no. 161.

161 Hilles, C., and Schmidt, L. H. Sulfanilamidopyridine (2-Para-Aminobenzenesulfonamidopyridine) in Experimental Infections with Type XXII Pneumococcus, *Proc Soc Exper Biol & Med* **40** 73-77 (Jan) 1939.

162 Raiziss, G. W., Severac, M., Moetsch, J. C., and Clemence, L. W. Comparative Effects of Sulfapyridine and Sulfanilamide in Type II Pneumococcic Infection of Mice, *Proc Soc Exper Biol & Med* **40** 434-435 (March) 1939.

In view of the reported good results observed from the use of sulfapyridine in the treatment of pneumonia, these authors found the results with experimental pneumococcic infection in mice less encouraging than with infection in man

COMPARATIVE THERAPEUTIC EFFECTS OF SULFAPYRIDINE IN EXPERIMENTAL STAPH AUREUS INFECTIONS IN MICE

Bliss and Long,¹⁶³ stated the opinion that the chemotherapeutic effect of sulfapyridine in staphylococcic infections in mice is definite enough to warrant careful clinical trial of the drug in cases of severe staphylococcic infection

LIMITATIONS OF ACTION OF SULFANILAMIDE IN CONTROL OF INFECTIVE LESIONS

1 So far as can be determined, sulfanilamide is of no therapeutic value against well developed abscesses. For such abscesses surgical drainage brought prompt relief.¹⁵¹

2 For necrotic lesions in which both hemolytic streptococci and hemolytic staphylococci were present, drug therapy was often ineffective even in the presence of free surgical drainage

3 Development of metastatic lesions and bacteremia occur. Lockwood, Coburn and Stokinger's¹⁵¹ observations suggest that (a) the protective action of sulfanilamide is greatest in the circulating fluids and that (b) bacteria remaining in necrotic tissues can become highly invasive after withdrawal of the drug

4 The organisms reappeared in many instances of hemolytic streptococcic infections, in some accompanied with relapse. In several patients hemolytic streptococcic metastatic lesions developed after sulfanilamide therapy had been stopped

5 Sulfanilamide therapy seemed most effective for rapidly spreading lesions in which there had been little tissue destruction. Lockwood and his associates cited the following case illustrating (a) the effectiveness of sulfanilamide in preventing invasion of infection into the meninges and (b) its inability to sterilize necrotic tissue

C S, aged 4 years, was admitted to the hospital because of intermittent earache and headache for three weeks. There was an extensive fluctuant swelling over the right parietal region. The right tympanum was white but was bulging posteriorly

Operation—A simple mastoidectomy was done on the right. The dural plate and the mastoid cells were soft. The dura was thickened and inflamed, and the brain beneath was soft

¹⁶³ Bliss, E A, and Long, P H. Comparative Therapeutic Effects of Sulfapyridine in Experimental Staphylococcus Aureus Infections in Mice, Proc Soc Exper Biol & Med **40** 32-34 (Jan) 1939

Culture of the pus from the epidural abscess showed a pure growth of hemolytic streptococci

Treatment with sulfanilamide was begun on the second day after operation and continued for three weeks (2.5 Gm a day)

The child was afebrile on the fourth and fifth days. However, the temperature began to rise at the end of the first week and continued to be elevated through the second week. A superficial incision released more pus, and the temperature fell to normal. The boy remained afebrile during the fourth week, after which sulfanilamide therapy was stopped. He was discharged after six weeks.

On the eleventh day at home he had a generalized convulsion lasting two minutes, the temperature was 104 F. The area previously operated on was explored for abscess of the brain, but none was found. Necrotic bone was removed from two sites, in each instance producing a pure culture of the hemolytic streptococcus.

Throughout the second stay at the hospital he received 2.5 Gm of sulfanilamide a day until the ninth week, when the dose was reduced to 2 Gm.

ACTION OF SULFANILAMIDES IN VITRO AND IN VIVO

All observers agree that the prontosils (the original prontosil and the more soluble preparation [azosulfamide]) even in high concentrations have no effect on the streptococcus in vitro. Indeed, Domagk's discovery of the effect of the original prontosil was due to his thought that it was possible that compounds which are not bactericidal in vitro might be so in vivo, and vice versa. However, with sulfanilamide in the form used at present, most observers are convinced that bacteriostatic or bactericidal effects can be demonstrated in vitro with concentrations of the drug equivalent to those occurring in the blood and tissues of patients undergoing treatment.¹⁶⁴

CLINICAL FACTS ABOUT SULFANILAMIDE

Reviewing the present status of chemotherapy of bacterial infections, Domagk's¹⁶⁵ experiments indicate (1) that the sulfanilamides are useless in the entirely hopeless cases in which there is no longer any power of reacting and (2) that a change in the cocci is always the primary factor, phagocytosis by leukocytes, monocytes and histiocytes being the secondary factor in the therapeutic action of the sulfanilamides.

Absence of Shock—Domagk made the important observation that (3) surgical shock is comparatively rare even after large intravenous doses, and that because shock is probably due to the rapid disintegration of too many cocci intramuscular injection should be preferred to intravenous injection.

164 Long, P. H., and Bliss, E. A. *The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds*, New York, The Macmillan Company, 1939.

165 Domagk, G. *Der derzeitige Stand der Chemotherapie der bakteriellen Infektionen* Ztschr. f. klin. Med. **136** 167-199, 1939.

HOW SULFANILAMIDE ACTS IN COMBATING INFECTION

The following hypotheses have been suggested to explain the mode of action of sulfanilamide in cases of hemolytic streptococcic infection

- 1 It stimulates phagocytosis
- 2 It neutralizes toxins
- 3 It acts by inhibiting the growth of organisms
- 4 It actually is bactericidal under certain conditions
- 5 It delays the growth of organisms until mononuclear phagocytes accumulate

6 The organisms are altered so that phagocytosis can take place (a) by the accumulation of hydrogen peroxide (H_2O_2) in the infected tissues, (b) through elevation of oxidation-reduction potentials (the symbol for which is rH), hydroxidized products having a greater electromotor force, and (c) by changes in the electromotor plateau equilibrium

Long and Bliss¹⁶⁴ stated the belief that up to the present time no theory has been evolved "which adequately explains the mode of action of these sulfur benzene derivatives" My own opinion is that the last-stated hypothesis—i e., that the organisms are altered so that phagocytosis can take place by elevated oxidation-reduction potentials (Shaffer) and that at times there are changes in the electromotor plateau equilibrium with accumulation of hydrogen peroxide in tissues (Shinn Main and Mellon)—is plausible and supported by established facts

How Infection Advances and How it is Influenced by Sulfanilamide

—The destruction of hemolytic streptococci in the body is a complex process and depends largely on the cooperative activity of a number of factors

(a) Sensitizing of Bacteria by an Antibody There is evidence that when the protective process is unaided by any serum or drug bacteria are first sensitized by an antibody

(b) Phagocytosis of Bacteria It is in this sensitized condition that phagocytosis of the bacteria can take place, for it is known that without the presence of an antibody the organisms grow freely and elaborate a substance (leukocidin) which destroys the leukocytes and another substance (hemolysin-streptolysin) which destroys the red blood cells

(c) Changes in Blood Plasma There is additional evidence that during febrile diseases not due to hemolytic streptococcic infection there is a change in the properties of the blood plasma that inhibits the growth of some strains of organisms This phenomenon has been described by Tillet¹⁶⁶ Its action has not been studied sufficiently in cases of hemolytic streptococcic infections in human beings to evaluate its relative importance in the defense mechanism of the body

¹⁶⁶ Tillet, W S The Bactericidal Action of Human Serum on Hemolytic Streptococci I Observations Made with Serum from Patients with Acute

(Footnote continued on next page)

REVIEW OF THE DIVERGENT VIEWS OF THE ACTION OF
SULFANILAMIDE IN INFECTIONS

Garrod ¹⁶⁷ stated the belief that sulfanilamide has a direct damaging action on the streptococci, either actually killing them or (at least) preventing their growth

The explanation advanced by Bliss and Long ¹⁶⁸ and by Gay and Clark ¹⁶⁹ is that bacteriostasis, if complete, ultimately results in the victory of the defense mechanism of the body Bliss and Long ¹⁶⁸ recently completed experiments which tend to show that the action of sulfanilamide on *Str haemolyticus* is bacteriostatic, retarding the growth and multiplication of the bacteria They expressed the opinion that it thus enables the host to overcome the infection

At the same time, somewhat similar experimental evidence was published by Gay and Clark ¹⁶⁹ Their conclusion was "Sulfanilamide apparently produces a bacteriostasis sufficiently marked to *protect the accumulated leukocytes* and to allow the natural defense macrophages to accumulate" The work of Mellon and his associates ¹⁷⁰ indicates that there is no stimulation of the defense mechanism in the sense of any altered behavior on the part of the leukocytes

Levaditi and Vaisman ¹⁷¹ stated the opinion that the original prontosil prevents capsule formation by streptococci, so rendering them susceptible to phagocytosis, Mayer and Vaisman claimed to have proved that it neutralizes streptococcus toxins (leukocidin and hemolysin)

Mayer ¹⁷² and Levaditi postulated the conversion of sulfanilamide itself in the body into some other and more active substance (see section on oxidation)

Infections and from Normal Individuals, *J Exper Med* **65** 147-161 (Jan) 1937,
II Factors Which Influence the Phenomenon in Vitro, *ibid* **65** 163-176 (Jan) 1937

167 Garrod, L P The Chemotherapy of Bacterial Infections, *Lancet* **1** 1125-1129 (May 14) 1933

168 Bliss, E A, and Long, P H Observations on the Mode of Action of Sulfanilamide, *J A M A* **109** 1524-1528 (Nov 6) 1937

169 Gay, F P, and Clark, A R On the Mode of Action of Sulfanilamide in Experimental Streptococcus Empyema, *J Exper Med* **66** 535-548 (Nov) 1937

170 Mellon, R R, Gross, P, and Cooper, F B Sulfanilamide Therapy of Bacterial Infections, Springfield, Ill, Charles C Thomas, Publisher, 1938
McKinney, R A, and Mellon, R R Sulfanilamide and Macrophage Response to Streptococcal Peritonitis in Mice, *Proc Soc Exper Biol & Med* **37** 333-336 (Nov) 1937

171 Levaditi, C, and Vaisman, A Action curative et preventive du chlorhydrate de 4'-sulfamido-2,4-diamino-azobenzene dans l'infection streptococcique experimentale, *Compt rend Acad d sc* **200** 1694-1696 (May 13) 1935

172 Mayer, R L Recherches sur le mecanisme de l'action antistreptococcique des phenylamines sulfamides, *Biol med, Paris (supp)* **27** 35 and 36, 1937,
Recherches sur le mecanisme de l'action antistreptococcique de l'aminobenzenesulfamide et de ses derives, *Bull Acad de med, Paris* **117** 727-735, 1937

From experiments on peritoneal washing in mice, Neter¹⁷³ stated "It may be concluded that the action of sulfanilamide on the hemolysin and fibrinolysin produced by hemolytic streptococci does not play a major part in the therapeutic effectiveness of the drug in streptococcal infections," for while the production of hemolysin by these organisms was delayed *in vivo*, this occurred only with concentrations of the drug above those usually encountered in patients treated with it¹⁷⁴

Lockwood and his associates¹⁵¹ said "It seems possible that sulfanilamide may alter the total metabolism of the microorganism or may interfere especially with some specific function, such as its capacity to digest protein"

Presence of Necrotic Tissue a Factor in Inhibiting Action of Sulfanilamide—In either case the presence of necrotic tissue appears to be of great importance. Sulfanilamide should be considered an agent which supplements, and in no way supplants, antibacterial immunity.

The effectiveness of sulfanilamide therapy is related to the type of lesion.

Presence of Antibodies Necessary in Action of Sulfanilamide—Keefer and Rantz¹⁷⁵ stated the belief that recovery from a hemolytic streptococcal infection depends on the mobilization of the body's defenses so that the effects of the bacteria can be neutralized. Once the defense mechanism gains the upper hand, a definite cure takes place.

They stated

There seems to be evidence that sulfanilamide in the tissue fluids inhibits and reduces the growth and rate of multiplication of hemolytic streptococci provided the concentration is above 7 mg per hundred cubic centimeters. In this way the defense mechanism of the tissues is allowed to mobilize in an effective manner. However, there is no evidence that this concentrated sulfanilamide destroys hemolytic streptococci through its direct action on the organism, nor is it clear that it stimulates either the accumulation of phagocytes or their activity.

But there is suggestive evidence that in the presence of antibodies more organisms may be destroyed when sulfanilamide is present than when it is not. This may be due to a reduction in the substances which neutralize the antibodies present and those which are being elaborated.

From their experiments Keefer and Rantz concluded that at least two conditions are essential for the optimum therapeutic action of sulfanilamide: (1) The drug must be present in sufficient concentration

173 Neter, E. Action of Sulfanilamide on Fibrinolysin and Hemolysin Produced by Streptococci *In Vivo*, Arch Path **26** 1082-1083 (Nov) 1938.

174 Meyer, F. Streptococcus Infection and Mechanism of Its Healing by Serum and Chemotherapy, Quart Bull, Sea View Hosp **21** 148-154 (Jan) 1937.

175 Keefer, C. S., and Rantz, L. A. Sulfanilamide. A Study of Its Mode of Action on Hemolytic Streptococci, Arch Int Med **63** 957-973 (May) 1939.

to produce optimum bacteriostasis, and (2) the body's defense mechanism must acquire or retain the power to destroy viable organisms

McIntosh and Whitby¹⁷⁶ (1939) stated that the sulfanilamide group of drugs seems to act by virtue of its bacteriostatic properties, which action is brought about by neutralization of some metabolic function of certain bacteria so as to interfere with their food supply¹⁷⁷

EXPERIMENTAL WORK ON CHEMOTROPISM OF SULFANILAMIDES

The purpose of Coman's¹⁷⁸ experimental work on "prontosil (a derivative of sulfanilamide, known as prontosil-soluble [the disodium salt of 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene 3'6'-disulfonic acid])," now known as azosulfamide, on sulfanilamide and on septazine (benzylsulfanilamide), which is less toxic than sulfanilamide, was to study the paths of leukocytes microscopically as the leukocytes moved in relation to solutions of these drugs. He stated that it is unlikely that the therapeutic effect of any of these drugs is due to an increase produced in the chemotropism of the leukocytes.

"Prontosil" (azosulfamide) did not significantly alter the chemotropic response of the leukocytes. Sulfanilamide in the concentration employed resulted in a cessation of cell movement. Septazine (benzyl sulfanilamide) caused only slight increase in the chemotropism.

Activation of the Reticuloendothelial System by Sulfanilamide—Davis, Harris and Schmeisser¹⁷⁹ found morphologic evidence of activation of the reticuloendothelial system by sulfanilamide, which, they stated, may provide a clue to its therapeutic activity.

White albino rats received subcutaneous injections of a 10 per cent suspension of sulfanilamide daily for three months. An increasing tolerance to the drug could be readily produced. At postmortem examination the bone marrow of the femurs showed mild hyperplasia of the myelopoietic (myelocytic) and erythropoietic (red cell) elements, with an increase in megakaryocytes (giant cells of the bone marrow). This accounted for the definite reduction of the number of erythrocytes and of the amount of hemoglobin, with slight leukocytosis in the peripheral blood during the life of the animal. At the site of injection there was proliferation of histiocytes, fibroblasts and numerous foreign body giant cells. Deposits of sulfanilamide crystals were found in the capsule of the liver and spleen and in the meninges. In several animals proliferation of the endothelium of the blood vessels of the liver was present, forming small nodular projections into the lumen.

176 McIntosh, J, and Whitby, L. E. H. The Mode of Action of Drugs of the Sulphonamide Group, *Lancet* **1** 431-435 (Feb 25) 1939

177 Cawthorne, T. Otogenic Meningitis, *J Laryng & Otol* **54** 444-470 (Aug) 1939

178 Coman, D. R. Effect of Substances of the Sulfanilamide Group on the Chemotropism of Leukocytes, *Arch Path* **25** 764-765 (May) 1938

179 Davis, H. A., Harris, L. C., Jr., and Schmeisser, H. C. Tissue Changes Following Prolonged Administration of Sulfanilamide in Rats, *Arch Path* **25** 750-751 (May) 1938

THE HYPOTHESIS THAT HEIGHTENED ELECTRODE POTENTIAL FROM
AN OXIDATION PRODUCT IS THE BACTERICIDAL AGENT OF
SULFANILAMIDE COMPOUNDS

On the basis of his observation that the oxidized form of hemoglobin, methemoglobin, frequently appears in the blood of patients and of animals treated with sulfanilamide, Mayer¹⁸⁰ suggested that the bactericidal effect of sulfanilamide is due to an oxidation product of the drug. He advanced the hypothesis that the oxidation product and not the sulfanilamide affects the bacteria. This is the same oxidation product which at the same time oxidizes hemoglobin, making it methemoglobin.

OXIDATION-REDUCTION ELECTRODE POTENTIALS AND OXYGENATION

Oxygenation is saturation with oxygen. The carrying of the oxygen by the blood to the tissues is performed by oxygenation of the hemoglobin, a reversible process, for, with the surrender of the oxygen to the tissues by the hemin, hemoglobin can again carry oxygen.

Oxidation is union with oxygen, oxidoreduction is an oxidation reaction considered from both the oxidizing and the reducing effects.

It is now conceded that oxidation of the tissues is an important "respiratory function" in the metabolic processes of all animals. Oxidation plays a large part in all metabolic processes¹⁸¹ and in the function of the central nervous system¹⁸².

Pasteur¹⁸³ was the first to contend that fermentation, e. g., of wines, is the result of the metabolism of specific micro-organisms¹⁸⁴.

Barron¹⁸⁵ explained that there exist in living cells three kinds of reversible oxidation-reduction systems: (1) electromotively active systems, which as a rule are oxidizable by atmospheric oxygen (hemochromogens, flavines and a number of other pigments), (2) sluggish reversible systems, which as a rule are not oxidizable by atmospheric oxygen (Warburg's coferment, glutathione, ascorbic acid), and (3) enzymatic oxidation-reduction systems (lactate-pyruvate, succinate-

180 Mayer,¹⁷² p. 727

181 Holmes, E. *Metabolism of Living Tissues*, London, Cambridge University Press, 1937, p. 36

182 Page, I. H. *Chemistry of the Brain*, Springfield, Ill., Charles C. Thomas, Publisher, 1937, p. 369

183 Pasteur, L. *Sur la fermentation visqueuse et la fermentation butyrique*, Bull. Soc. Chim., February 1861, vol. 8

184 Stephensen, M. *Bacterial Metabolism*, New York, Longmans, Green & Co., 1939

185 Barron, E. S. G. *Studies on Biological Oxidations. IX. The Oxidation-Reduction Potentials of Blood Hemin and Its Hemochromogens*, J. Biol. Chem. **121** 285-311 (Oct.) 1937

fumarate) The systems belonging to the first group act as the oxidizing catalysts of biologic oxidations "For the conversion of hemin into a hemochromogen is accompanied by an increase in the electroactivity of the system and in the value of the oxidation-reduction potential" (Barron)

Oxygenated Hemins—The name hemochromogen is used to indicate complex compounds of heme and nitrogenous constituents, which are electromotively active reversible oxidation-reduction systems

Warburg and Negelein¹⁸⁶ classified hemins in three groups (1) red hemins (blood hemin and its derivatives, coprohemin, pyrohemin, phyllohemins, and rhodohemin), (2) green hemins (pheophorbide hemins), and (3) mixed dichroic hemins (*Spirographis* hemin) These groups are easily characterized by the spectroscopic properties of their ferrochemochromogens

Oxygen Necessary for the Action of Sulfanilamide on Bacteria—The presence of oxygen is important in the action of the sulfanilamides, as "both (sulfanilamide and sulfapyridine) are wholly without effect on the growth of bacteria in the absence of oxygen" All the tissues of the body normally possess a protective mechanism against oxidation Shaffer¹⁸⁷ stated

The organisms are killed by such excess of active oxidant as will maintain the oxidation potential (Eh) above a critical level

Both drugs become more or less bacteriostatic or bactericidal under certain aerobic conditions but promptly lose this property when the culture media become anaerobic in consequence of bacterial metabolism and the resulting consumption of dissolved oxygen

As the oxygen supply of the body tissues is regulated by the oxygen-carbon dioxide tension, decrease in oxygen tension in the tissues is accompanied with diminished inhibition of growth caused by sulfanilamide

Uninoculated sterile broth containing sulfanilamide exhibited higher oxidation-reduction potentials than broth without the drug This difference was in the region of 50 millivolts The drug will change the potential of sterile mediums The time-potential curves obtained for streptococcic cultures were consistently higher when they contained sulfanilamide in a concentration of 1:10,000 This elevation reached a maximum at about the tenth hour The maximal levels were about

186 Warburg, O., and Negelein, E. Ueber das Hemin des sauerstoffübertragenden Ferments der Atmung, über einige künstliche Hamoglobine und über *Spirographis*-Porphyrin, *Biochem Ztschr* **244** 9-32, 1932

187 Shaffer, P. A. The Mode of Action of Sulphanilamide, *Science* **89** 547-550 (June 16) 1939

80 to 100 millivolts more positive than cultures without the drug, and this difference was maintained for seventy-two hours

This difference in potential could be ascribed to a diminished rate of growth of the organism

Increase in the Sterilizing Intensity of Molecular Oxygen by Sulfanilamide—Continuing the oxidation-reduction hypothesis, the results of Shaffer's study of oxidation-reduction potentials suggest that "sulfanilamide provides a mechanism by which the sterilizing oxidation intensity of molecular oxygen is applied to bacteria nearly at its maximum"—at the same time as well, to the cells of the body, where the drug oxidizes the hemoglobin, which latter causes cyanosis by methemoglobin and occasionally by sulfhemoglobin (Hartmand, Wendel, Watson and others¹⁸⁸)

Elevation of the Oxidation-Reduction Potential in Sulfanilamide Bacteriostasis—Sulfanilamide is not an oxidant and is itself inactive toward electrodes. However, sulfanilamide and sulfapyridine are readily oxidized by a number of chemical oxidants as well as by electrolytic oxidation. The primary end product of this oxidation process seems to be nitrosobenzenesulfonamide. The oxidized products are highly reactive, they are promptly reduced by oxyhemoglobin.

For when even a very small fraction of a sulfanilamide product is oxidized in a culture medium or in the tissue (as it may be by a ferric or ferrous ion present in the serum or in the tissues or by hydrogen peroxide [H_2O_2] resulting from the metabolism of bacteria), the oxidized product imposes a higher electric potential, that is, the capacity to produce electric effects in bodies which are in different states of electrical equilibrium. For when two areas of tissues of different potentiality, such as occurs in infections, are brought near each other, electrode changes are set up between them.

"The measured potentials of oxidized sulphanilamid solutions indicate an astonishingly high oxidizing intensity for these products." "At p_H 4.6 the plateau potential (Eh) of sulphanilamide oxidant is +0.59 v." At p_H 7 it is +0.45 v, "which is considerably higher than the normal potential of any other organic substance yet measured (except sulphapyridin and adrenalone)." (Shaffer) (Adrenalone is the ketone of epinephrine.)

Shaffer stated "For the potential measurements I am indebted to Dr. E. S. Hill."

"Approximate agreement of potentials is obtained with different oxidizing agents at the same p_H levels. Presumably these potentials

188 Watson, C. J., Vigness, I., and Spink, W. W. Relation of Methemoglobin to the Cyanosis After Sulfanilamide, *Proc. Soc. Exper. Biol. & Med.* **40**: 547-548 (April) 1939.

represent characteristic intensity levels of the substances from which the products are formed" (It is fair to assume, therefore, that in the tissues of the body they have a similar action to that experimentally obtained—W P E)

Again, the measured potentials of oxidized sulfanilamide solutions indicate an astonishingly high oxidizing intensity for the reversible electrode couple, which is composed of the hydroxyl amine and its nitroso derivatives, or of the corresponding semiquinone-free radicals

Action of Elevated Oxidation Potential on Bacterial Growth in Culture Mediums—Many active oxidizing agents possessing sufficient oxidizing intensity are highly bactericidal to many organisms, provided, however, that this sterilizing oxidation is not diverted from the bacteria to the reduction of other oxidizable substances that are in the culture fluid (Shaffer)

Thus the bactericidal action of normal human serums on the streptococcus operates at an optimum if oxidation-reduction conditions are avoided (Tillett and Stock¹⁸⁹)

In the presence of air (21 per cent oxygen) the inhibition of growth of the bacteria is 54 per cent, at a level of 10 per cent oxygen it is 40 per cent, and the decrease continues until a concentration of 1 per cent oxygen is reached, at which point the inhibition is essentially zero

The stimulus and the recurring inhibition at the lowest values are interpreted as evidence of the formation of a toxic reduction compound, possibly a sulfide. This type of inhibition may play a role in any bacteriostatic effect against anaerobes

Dubos¹⁹⁰ has shown that the bacterial growth in vivo of streptococci and pneumococci is inhibited if the rH^{190a} is maintained above a critical

189 Tillett, W S, and Stock, C C. Bactericidal Action of Human Serum on Hemolytic Streptococci, Studies Concerning Significance of Hydrogen Ion Concentration in Relation to Streptococcal Action of Serum, Effect of Reducing Agents on Phenomenon, J Exper Med **66** 617-636 (Nov) 1937

190 Dubos, R. Relation of Bacteriostatic Action of Certain Dyes to Oxidation-Reduction Processes, J Exper Med **40** 575-592 (April) 1929

190a The rH is the symbol for oxidoreduction potential of the system in which the micro-organic growth is taking place. For it must be appreciated that each system of an oxidizing medium has an individual intensity level expressed by the constant rH

$rH = \log \frac{1}{p_{H_2}}$, p_{H_2} being the hydrogen pressure in atmospheres

p_H is the symbol representing the electric potential of the hydrogen ion when in contact with hydrogen. The p_H is the logarithm of the reciprocal of the hydrogen ion concentration, $p_H = \log 1/C_{H^+}$

In the body fluids $p_H 7$ represents neutrality, or equilibrium, $p_H 5$, acidity (acidosis), and $p_H 9$, alkalinity (alkalosis)

level by the introduction, at frequent intervals, of a soluble dye stuff, such as oxidized indophenol, or of a small quantity of iodine (or chloro compounds)

Conditions in the Tissues Hindering the Development of Oxidation Products of the Sulfanilamides—According to Fox, German and Janeway,¹⁹¹ “a dominant reduction environment,” consisting of (a) a free blood supply, (b) a low oxygen tension, (c) active metabolism and (d) a high catalase content, protects the tissues from the sulfanilamide oxidation products, this is because the free oxygen is consumed by the active oxygen-reducing substances in the tissues

Such environment is simulated in vitro when iodine is added slowly to a culture of bacteria, under these conditions no deleterious effects occur on a growing culture long after the lethal dose of iodine has been passed. This is because the slow oxidation has prevented the iodine ions (I_2) from ever being liberated in sufficient amount to affect the bacteria, there never occurring an excess of iodine ions with a rise of the oxidation electrode potential above that previously in the culture mediums (Clark)

Sulfanilamide Oxidants in Culture Mediums—Prontosil (disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3',6'-disulfonate) is inactive in vitro unless reduced to sulfanilamide before being added to the culture (Warren, Street and Stokinger)¹⁹³

The oxidation-reduction potential of a culture medium induced by sulfanilamide caused an elevation of the electromotor force (E M F) from a 210 millivolt optimum to less than 50 millivolts, depending partially at least on the presence of reducing agents in the culture (Warren, Street and Stokinger)¹⁹³

It has been demonstrated (1) that the addition of sulfanilamide to sterile broth is accompanied by an elevation of the oxidation-reduction potential and (2) that during sulfanilamide bacteriostasis an elevated electrode potential occurs in the culture mediums. Thus sulfanilamide added to broth raises the oxidation-reduction electrode potential. Furthermore, addition of sulfanilamide delays somewhat the fall of the electrode potential (Eh) that usually occurs as growth of bacteria proceeds (Fox, German and Janeway¹⁹¹)

Warren, Street and Stokinger found (3) that the rise of Eh can be eliminated when *Streptococcus haemolyticus* is grown anaerobically

191 Fox, C L, German, B, and Janeway, C A Effect of Sulfanilamide on Electrode-Potential of Hemolytic Streptococcal Cultures, *Proc Soc Exper Biol & Med* **40** 184-189 (Feb) 1939

192 Footnote deleted

193 Warren, J, Street, J A, and Stokinger, H E Influence of Sulfanilamide and Related Compounds Upon Oxidation-Reduction Potentials of the Hemolytic *Streptococcus*, *Proc Soc Exper Biol & Med* **40** 208-212 (Feb) 1939

(Warren Street and Stokinger, 1939) They also found (4) that compounds related to sulfanilamide but without bacteriostatic action do not affect the oxidation-reduction potential of the culture

Prediction of the Future Forms of Chemotherapy Useful for Bacterial Control—Shaffer concluded his important contribution with this statement "If the ideas here advanced are even in part correct, the new era of bacterial chemotherapy will deal with (1) oxidation-reduction potentials, (2) with the relation of molecular structure of organic substances to potential levels, and (3) with the immediate oxidation stages of nitrogenous compounds"

Shaffer further stated about the future type of drugs for the control of infections

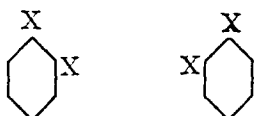
1 If high potentials are desired, 'ortho-' rather than 'para-' substitution of the oxidizable group may be preferred¹⁹⁴

2 It is unlikely that this sulfonic acid group is essential to activity, though it does raise potentials and increases solubility

3 Hydroxyl (HO) rather than amino (NH₂) compounds may be useful

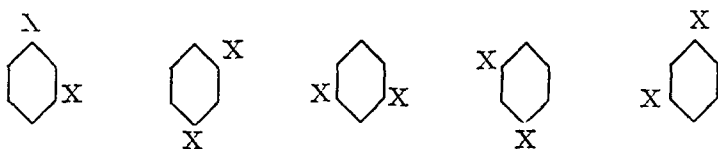
194 The di-substitution products of benzene exist in three isomeric forms

Ortho- is a prefix indicating the neighboring straight or normal and one among, or 1 2 positions. Thus, ortho- compounds indicate the substitution of atoms or groups in the 1 2 position to one another, or arranged consecutively, i e, linked to two adjacent carbons



The ortho- cyclic derivatives of the benzene ring are those substances formed by the substitution of two adjacent hydrogen atoms

Meta- is a prefix which in Greek means after or between or over. It denotes compounds with the substituting atoms or groups occupying the 1 3 position or linked to the first and third, the first and fifth, the second and fourth, the third and fifth or the fourth and sixth carbon atoms in the benzene ring



Para- (alongside, near, or beyond) Para derivatives are formed by the substitution of two atoms of hydrogen situated opposite to each other, i e, linked to opposite carbon atoms



An important addition to this prediction is Cohn's survey¹⁹⁵ of the present knowledge of the nature of the polar and nonpolar side chain group of proteins (Marrock,¹⁹⁶ Cohn¹⁹⁷)

Cohn¹⁹⁸ called attention in 1934 to the fact that there is in addition to the usual ions, what the Germans call a "zwitter ion" in certain proteins (a zwitter ion being a complex ion that is both positively and negatively charged) Cohn states that the term "dipolar ion" has been adopted, although it is not an ideal description of the class of molecules

The dielectric constant measurements of the aliphatic amino acids indicate that their electrical properties are essentially the same¹⁹⁹

ANTICATALASE THEORY RELATIVE TO THE ACCUMULATION OF HYDROGEN PEROXIDE IN THE TISSUES

ANTICATALASE ACTIVITY OF SULFANILAMIDE AND RELATED COMPOUNDS, OXYGEN TENSION AND BACTERIOSTASIS IN PNEUMOCOCCIC CULTURES

The theory that the retardation of growth of certain micro-organisms in the presence of sulfanilamide may be primarily the result of the accumulation of hydrogen peroxide (H_2O_2) was originally proposed by Locke and his associates^{199a} The accumulation of hydrogen peroxide is presumed to arise through inhibition of the normal catalase by the presence of sulfanilamide activated by oxidation

Catalase is an enzyme capable of decomposing hydrogen peroxide in the tissues, thus liberating free oxygen (O_2)

195 Cohn, E J Proteins as Chemical Substances and as Biological Compounds, *Bull New York Acad Med* **12** 639-667 (Oct) 1939

196 Marrock, J R The Chemistry of Antigens and Antibodies Inter-molecular (Polar) Forces and the Electronic Theory of Valency, Medical Research Council, Special Report Series, no 194, London, His Majesty's Stationery Office, 1934

197 Cohn, E J The Physical Chemistry of the Proteins, *Physiol Rev* **5** 349-437 (July) 1925

198 Cohn, E J Influence of the Dielectric Constant in Biochemical Systems, *Chem Rev* **19** 241, 1936, Some Physical-Chemical Characteristics of Protein Molecules, *ibid* **24** 203, 1939 Cohn, E J, McMeekin, T L, and Blanchard, M H Studies in Physical Chemistry of Amino Acids, Peptides and Related Substances XI The Solubility of Cystine in the Presence of Ions and Another Dipolar Ion, *J Gen Physiol* **21** 651-663 (May) 1938, *Compt rend d trav d lab de Carlsberg, serie physiol* **22** 142, 1938 Cohn, E J Number and Distribution of the Electrically Charged Groups of Proteins, in *Cold Spring Harbor Symposia on Quantitative Biology*, Cold Spring Harbor, L I, New York, The Biological Laboratory, 1938, vol 6, p 9

199 Smith, P K, and Smith, E R B Thermodynamic Properties of Solutions of Amino Acids and Related Substances II The Activity of Aliphatic Amino Acids in Solution at Twenty-Five Degrees, *J Biol Chem* **121** 607-613 (Nov) 1937

199a Locke, A, Main, E R, and Mellon, R R Anticatalase and Mechanism of Sulfanilamide Action, *Science* **88** 620-621 (Dec 30) 1938

Catalase is the first enzyme isolated which contains a protein with iron—a hematin or a substance closely related to hematin²⁰⁰

Peroxi-dases do not play an important role in animal oxidations. In the normal metabolic process the hydrogen peroxide is removed or destroyed as fast as it is produced. Hydrogen peroxide (H_2O_2) is fairly toxic.

It is formed as a by-product in the action of xanthine oxidase on xanthine (one of the steps of the transformation of purines into uric acid). However, if the enzyme is inhibited the reaction ceases²⁰¹

Sulfanilamide and many structurally related compounds have an appreciable anticalase activity, which is frequently enhanced by oxidative processes, such as those involved in ultraviolet irradiation. The bacteriostasis of the type I pneumococcus in vitro is accompanied by a correspondingly marked accumulation of hydrogen peroxide in the culture.

Hydrogen peroxide in the presence of ferric (Fe^{+++}) and ferrous (Fe^{++}) ions—which are present in serum and in the tissues—is a rapid oxidant of sulfanilamide.

"Sterling of Bacteria in Their Own Juice" of Hydrogen Peroxide Because of Inactivation of Catalase by Sulfanilamide—As has been stated, oxygen plays a vital role in the action of sulfanilamide and as free oxygen (O_2) is poisonous to strictly anaerobic bacteria. Shinn, Main and Mellon²⁰² suggested that oxygen exerts its influence through the agency of the hydrogen peroxide.

The anticalase activity of sulfanilamide apparently depends on activation of the para-amino group (Shinn, Main and Mellon). Sulfanilamide is not an oxidant and is itself inactive toward electrodes, but when even a very small fraction is oxidized the product imposes a high potential.

Thus, in the presence of bacterial infection with the production of hydrogen peroxide (H_2O_2), Shinn, Main and Mellon suggested that catalase would be more or less inactivated by substances which may be oxidized even slightly into reactive products with high potentials. Once the oxidation process is slowly started, toxic oxidation products are formed in proportion as free oxygen is available, and hydrogen peroxide is produced.

200 Sumner, J. B., and Dounce, A. L. Crystalline Catalase, *J. Biol. Chem.* **121** 417-424 (Nov.) 1937.

201 Holmes,¹⁸¹ pp. 59-60.

202 Shinn, L. E., Main, E. R., and Mellon, R. R. Anticalase Activity of Sulfanilamide and Related Compounds. III. Oxygen Tension and Bacteriostasis in Pneumococcal Cultures, *Proc. Soc. Exper. Biol. & Med.* **40** 640-645 (April) 1939.

The oxidation products of sulfanilamide caused by radiation (Ottenberg and Fox) destroy catalase. This allows the hydrogen peroxide to accumulate in respiring bacterial cultures. From this, Shinn and his co-workers advanced the hypothesis that the bacterial action is due to the hydrogen peroxide.

They stated that

Certain types of germs first manufacture hydrogen peroxide—which is very unstable. This the germs utilize as a source for the oxygen which they must breathe to live. In order for the germs to obtain oxygen in a form acceptable to them, they must first convert the oxygen of the air into hydrogen peroxide. From this substance they obtain their oxygen by feeding from the water, which is a part of the peroxide molecule. This change can be effected only by the enzymes known as catalase.

Sulfanilamide, by inactivating or poisoning the catalase, prevents the breakdown of the hydrogen peroxide, which then accumulates within the bacterial cell. Now hydrogen peroxide is in one sense a waste product of the bacteria and as such is poisonous to them. So sulfanilamide, by making possible the accumulation of this waste product, virtually permits the bacteria to "stew in their own juice."

EVIDENCE AGAINST THE ANTICATALASE THEORY

Warren, Street and Stokinger¹⁹³ expressed the opinion that the fact that "elevations of the oxidation-reduction potentials were present in plain broth" is against Shinn, Main and Mellon's hypothesis ("the increased oxidation-reduction potential is due to an interference with the catalase activity of the tissues, with an accumulation of peroxides"), for it is difficult to explain the inhibition of bacterial growth at low oxygen tension as a result of accumulation of peroxide. They stated, however, that "sulfanilamide inactivates enzymic systems, in combination with sulphydryl and other groups normally responsible for the attainment of *highly negative reduction potentials*."

There is little definite knowledge of the specific oxidation-reduction system in living tissues, because but a small number of these systems are amenable to direct potentiometric study (Ball and Chen²⁰³) in which systems "special derivatives of ortho- and para-dihydroxybenzene are the reductants." These derivatives occur as the anomalous products of animal metabolism or as hormones or poisons in animal life. "In plants they are associated with oxidative catalysis and defense mechanisms against infection."

It is of particular interest that the oxidants of practically all these compounds are unstable, especially in solutions having a p_H within the physiologic range and above. Therefore, if these compounds are to be

203 Ball, E. G. and Chen, T.-T. Studies on Oxidation-Reduction XX
Epinephrine and Related Compounds, J. Biol. Chem. **102** 691-717 (Oct) 1933

protected from a virtually destructive oxidation in those natural environments which are reputed to be the seats of vigorous oxidative processes, the level of intensity at which the general oxidative processes proceed must be below the level required for the oxidation of these specific substances

The potentials of the naturally occurring systems are found to be so positive that living tissues under normal physiologic conditions can keep them practically completely in the reduced state. The reductants of these systems are thereby protected from a virtually destructive oxidation (Ball and Chen)

NERVOUS MANIFESTATIONS OF TOXICITY OF SULFANILAMIDE ²⁰⁴

VESTIBULAR DYSFUNCTION

Long and Bliss ²⁰⁵ demonstrated that large doses of sulfanilamide administered to mice produce symptoms of bilateral vestibular dysfunction associated with a curious spastic paralysis

BLINDNESS AND OPTIC NEURITIS

Custer ²⁰⁶ produced blindness, ataxia and spastic paralysis in dogs. In a girl of 16 years receiving acetylsalicylic acid, phenobarbital and ferrous sulfate (previously noted to be a contraindication), Bucy ²⁰⁷ observed blurring of the margin of the optic disks and reduction of vision from a central scotoma, with cyanosis, under sulfanilamide therapy

UNUSUAL REACTIONS FOLLOWING CHEMOTHERAPY

SULFANILAMIDE, A PHOTSENSITIZING AGENT

The synergistic action of sunlight and sulfanilamide in producing a well defined rash was noted by Newman and Sharlit ²⁰⁸ in 4 cases

Experimental injection of sulfanilamide in conjunction with ultraviolet irradiation resulted in a similar rash. Thus, it appears obvious that sulfanilamide can produce a definite photosensitizing effect on the skin

204 Long, P. H., and Bliss, E. A. Toxic Manifestation of Sulfanilamide, *Ann Surg* **108** 808-812 (Nov.) 1938

205 Long, P. H., and Bliss, E. A. Para-Amino-Benzene-Sulfonamide and Its Derivatives. Experimental and Clinical Observations on Their Use in Treatment of Beta-Hemolytic Streptococcal Infection, Preliminary Report, *J. A. M. A.* **108** 32-37 (Jan. 2) 1937

206 Custer, R. P., Forster, H. W., Lamotte, W. O., Patton, D. M., and Phinney, J. D. Changes in the Central Nervous System in Sulfanilamide Intoxication, *Arch. Path.* **26** 904-905 (Oct.) 1938

207 Bucy, J. C. Toxic Optic Neuritis Resulting from Sulfanilamide, *J. A. M. A.* **109** 1007-1008 (Sept. 25) 1937

208 Newman, B. A., and Sharlit, H. Sulfanilamide. A Photosensitizing Agent of the Skin, *J. A. M. A.* **109** 1036-1037 (Sept. 25) 1937

The rash, which consisted of scattered macular plaques, varying in size, was confined to an area of the body which had been exposed to ultraviolet rays. Sunlight was its cause. The boundaries of the clothing sharply demarcated the area occupied by the rash from the rest of the body.

PIGMENT METABOLIC DISTURBANCE FROM SULFANILAMIDE DUE TO A DEEP-SEATED EFFECT ON THE HEMOPOIETIC SYSTEM

Rimington²⁰⁹ stated

It has been postulated that the sulphanilamide possibly acts by interfering with the mechanism for the incorporation of iron into photoporphyrin to produce hematin, and that photosensitizing pigments are liberated in the organism as a result of sulfanilamide therapy.

The available evidence would suggest that a certain degree of blood-cell destruction is caused by sulfanilamide in the doses employed, but the disturbance in pigment metabolism is not to be explained by this fact alone. A more deep-seated effect upon the hematopoietic system possibly analogous, in some ways, to the toxic action of lead is suspected.

Porphyrin—a Red Decomposition Product of Hematin Containing No Iron^{209a}—*in the Photosensitivity Rashes from Sulfanilamide*—Nine of Hageman and Blake's²¹⁰ 134 patients after the use of sulfanilamide had a maculopapular erythema of wide distribution, with a resemblance to the rash due to serum sickness. However, there was no evidence of sensitization to sulfanilamide. (These authors think that the accompanying fever probably is a reaction to the products of lysed bacteria.)

There are several other American reports of the condition (Schwentker and Gelman²¹¹), mainly of its occurrence in ambulatory patients with gonorrhea, some of whom had been taking sun baths.

Photoallergic Element in Sulfanilamide—Epstein²¹² found that sulfanilamide produces a primary photosensitivity at the site of intracutaneous injection. The experiments demonstrate a true allergic type of photosensitivity (photoallergy). The author stated the opinion that this is the first report of this particular type of photosensitization and the first experimental proof of the allergic nature of this form of light sensitivity.

209 Rimington, C. Porphyrinuria Following Sulphanilamide, Sulphanilamide Dermatitis, *Lancet* **1** 770-776 (April 2) 1938.

209a Porphyrin is not mentioned by Hageman and Blake. This is my own deduction.—W. P. E.

210 Hageman, P. O., and Blake, F. G. Specific Febrile Reaction to Sulfanilamide. *Drug Fever*, *J. A. M. A.* **109** 642-646 (Aug. 28) 1937.

211 Schwentker, F. F., and Gelman, S. Sulfanilamide Rash, *Bull. Johns Hopkins Hosp.* **61** 136-139 (Aug.) 1937.

212 Epstein, E. Photoallergy and Primary Photosensitivity to Sulfanilamide, *J. Invest. Dermat.* **2** 43-51 (April) 1939.

The injection followed by an erythema dose of ultraviolet rays produced the reaction in all 22 patients. In 2 of the patients a different type of reaction appeared on the tenth day, which developed spontaneously at the site of the primary reaction. It was an inflammatory urticarial reaction with intense pruritus, while the primary eruption had consisted of an erythema of about 0.8 to 1 cm in diameter, contrasting with the milder erythema of the surrounding skin. Every subsequent experiment on the sensitized persons produced a spontaneous inflammatory urticarial response, which appeared not ten days but from ten to twenty-four hours after the test.

ACIDOSIS FROM SULFANILAMIDE

Southworth²¹³ reported 2 cases of clinical acidosis due to sulfanilamide.

CASE A—Acute tonsillitis due to a beta hemolytic streptococcus was present, sulfanilamide was given. The temperature fell to normal in twenty-six hours. However, after forty-eight hours the patient had overbreathing, and the carbon dioxide-combining power of the blood plasma²¹⁴ was 32.2 volumes per cent. (Two months later, she took 6.9 Gm of sulfanilamide in sixty hours, and there was no definite clinical evidence of acidosis.)

CASE B—Wound infection following craniotomy was present, sulfanilamide was given by mouth, and an 0.8 per cent solution of the drug was administered both subcutaneously and intrathecally (averaging about 4 Gm or 0.06 to 0.07 Gm per kilogram of body weight, per day). After six days Kussmaul breathing, "air hunger"—the dyspnea of diabetic coma (deep and sighing)—occurred, with a carbon dioxide-combining power of 31.5 volumes per cent. Later this value fell to 27.17 volumes per cent.

Fifteen consecutive patients who were treated similarly showed a consistent though variable drop in the carbon dioxide-combining power of the blood plasma. The mechanism of the acidosis is as yet unknown.

Cyanosis from Sulfanilamide—Cyanosis occurs in over 60 per cent of all patients who receive sulfanilamide. It is not accompanied by the dyspnea of diminished oxygen-carrying capacity of the blood.²¹⁵ Sulfhemoglobinemia or methemoglobinemia was at first regarded as the cause of cyanosis.²¹⁶ It has been thought that the sulfhemoglobinemia is

213 Southworth, H. Acidosis Associated with the Administration of Para-Amino-Benzene-Sulfonamide (Prontylin), *Proc Soc Exper Biol & Med* **36** 58-61 (Feb.) 1937.

214 The range of the normal carbon dioxide-combining power of the blood is from about 45 to 55 cc per hundred cubic centimeters of blood.

215 Marshall, E. K., Jr., and Walzl, E. M. On Cyanosis from Sulfanilamide, *Bull Johns Hopkins Hosp* **61** 140-144 (Aug.) 1937.

216 (a) Colebrook, L., and Kenny, M. Treatment of Human Puerperal Infections and of Experimental Infections in Mice with Prontosil, *Lancet* **1** 1279-1286 (June 6) 1936, (b) Treatment with Prontosil of Puerperal Infections Due to Hemolytic Streptococcus, *ibid* **2** 1319-1322 (Dec. 5) 1936.

due to administration of sulfates,²¹⁷ generally in the form of magnesium sulfate. The real cause of the cyanosis is unknown, but it may possibly result from the action of a black oxidation product of the drug on the surface of the red blood cells.²¹⁵

Relation of Methemoglobin to the Cyanosis Occurring After Administration of Sulfanilamide—Two explanations have been offered for the cyanosis often noted after administration of sulfanilamide. The first is that the drug causes formation of methemoglobin or (secondarily, because of the presence of sulfur) of sulfhemoglobin. The second explanation is that a black or blue pigment derived from sulfanilamide occurs in the blood and produces cyanosis.

Watson, Vigness and Spink¹⁸⁸ expressed the conviction that the cyanosis due to sulfanilamide is caused in all instances by methemoglobin (rarely sulfhemoglobin). Their results confirm the conclusions of Hartman and his associates, as well as the recent findings of Wendel, that methemoglobin (or sulfhemoglobin) is the cause of sulfanilamide-induced cyanosis and that methylthionine chloride (methylene blue) given intravenously rapidly abolishes the methemoglobinemia.

In Campbell and Morgan's²¹⁸ experience with sulfanilamide (paraaminobenzenesulfonamide) and sulfapyridine (2-[paraaminobenzenesulfonamide]-pyridine), cyanosis has been a frequent symptom. With the former compound the pigment may be either methemoglobin or, less frequently, sulfhemoglobin. With sulfapyridine it is practically always methemoglobin. Cyanosis due to sulfhemoglobin lasts several weeks, that due to methemoglobin, a few days only. It is difficult to distinguish between these two pigments by spectroscopic examination of the blood, because characteristic absorption bands of both lie in the same vicinity of the end of the spectrum.

Two precautions are necessary in detecting the presence of methemoglobin: (1) The blood should be diluted with a small volume of water (not more than 1:5), and (2) the specimen should be examined soon after withdrawal.

Methylthionine chloride (methylene blue) is effective in causing the rapid disappearance of the cyanosis by converting methemoglobin to hemoglobin. As to the formation of sulfhemoglobin, it is possible that aniline derivatives are changed in the tissues to paraaminophenol, leading primarily to the formation of methemoglobin. However, in the presence of sulfide the latter combines with the iron hemoglobin in the ferric state and gives rise to sulfhemoglobin.

²¹⁷ Marshall, E. K., Jr., Emerson, K., Jr., and Cutting, W. C., cited by Colebrook and Kenny.^{216b}

²¹⁸ Campbell, D., and Morgan, T. M. Cyanosis Caused by Sulphonamide Compounds, *Lancet* 2:123-127 (July 15) 1939, abstracted, *Neuro-Psychiatric Institute of the Hartford Retreat*, series 7, no. 164.

SODIUM BICARBONATE AND SODIUM LACTATE IN PREVENTION OF ACIDOSIS

As cyanosis of varying degrees is nearly a constant finding in reactions from sulfanilamide, Long and Bliss²⁰⁴ began routinely to prescribe sodium bicarbonate with each dose of sulfanilamide (in amounts one-third to one-half the dose of the latter drug). Since the institution of this treatment the incidence of clinical acidosis has been materially reduced.

If sulfanilamide is to be given by parenteral injection, the use of one-sixth molar sodium lactate²¹⁹ as the solvent will prevent the development of acidosis.

ACUTE HEMOLYTIC ANEMIA ASSOCIATED WITH AUTOAGGLUTINATION FOLLOWING ADMINISTRATION OF SULFANILAMIDE FOR SORE THROAT

Antopol and his associates²²⁰ reported the following case:

CASE 2—History—A boy aged 5 years complained of severe sore throat five days prior to his admission to the hospital. His temperature was 104 F. Two days prior to admission he was given 90 Gm of sulfanilamide in thirty-six hours. On the following day there developed acute anemia and gray buccal patches.

On admission the laboratory examination furnished evidence of moderately severe acute hemolytic anemia with hemoglobinuria. Blood typing showed that the erythrocytes were strongly agglutinated by both A and B serums, suggesting group AB. Red cells were agglutinated by his own serum at room temperature. These agglutination phenomena disappeared after incubation at 37 C, and his blood was found to belong to group O.

Treatment—The patient was given 350 cc of blood and an infusion of 5 per cent dextrose in saline solution. Daily transfusions were given for four days, in amounts varying from 300 to 350 cc.

Course—The erythroid picture remained constantly low despite the daily infusion of blood until the fifth day, when it showed a prompt rise.

Recovery was rapid.

DEATH FROM ACUTE HEMOLYTIC ANEMIA FOLLOWING TREATMENT WITH SULFANILAMIDE

There have been 2 deaths from "acute hemolytic anemia" (active destruction of red blood cells in the circulation) following administration of sulfanilamide, from doses of the drug which were not excessive.

Hemolytic anemia is characterized at autopsy by iron pigmentation of the liver and spleen, pallor of the viscera and generalized icterus.

Koletsky's²²¹ (1939) patient, after mastoidectomy for infection with the pneumococcus type III, received 24 Gm of sulfanilamide in four

²¹⁹ Molar solution represents one containing 18.67 Gm per liter of sodium lactate.

²²⁰ Antopol, W., Applebaum, I., and Goldman, L. Two Cases of Acute Hemolytic Anemia with Auto-Agglutination Following Sulfanilamide Therapy, *J A M A* **113** 488-489 (Aug 5) 1939.

²²¹ Koletsky, S. Fatal Hemolytic Anemia Following the Administration of Sulfanilamide, *J A M A* **113** 291-294 (July 22) 1939.

days, and Wood's²²² (1938) patient, with streptococcic pneumonia, was given 44.7 Gm in five days

Both patients were adults, and both had had syphilis years previously. This raises the question whether syphilis, which often affects the hemopoietic system (as indicated by the frequent development of secondary anemia) may not have caused some alteration in the hemopoietic apparatus and thus have been the real cause of death.

In Koletsky's case the Wassermann and Kline reactions were strongly positive, and syphilitic aortitis was observed at autopsy. In Wood's case the patient gave a history of syphilis and had received fairly adequate antisyphilitic therapy about eight years prior to the present illness. On admission the Wassermann reaction was negative, while the Kline diagnostic and exclusion tests gave strongly positive results.

In Koletsky's case an autopsy revealed erythropoietic hyperplasia (overactivity) of the bone marrow. Erythropoietic hyperplasia of the marrow is the usual secondary reaction when peripheral hemolysis of the red blood cells occurs. It showed that the sulfanilamide did not attack the bone marrow, which at the time of death was still overactive.

The hemolytic anemia apparently resulted from destruction of the blood cells in the peripheral circulation. The sulfanilamide destroyed the red blood cells directly or by exerting an indirect effect through the reticuloendothelial system. This form of hemolytic reaction has been attributed to drug idiosyncrasy.

The following observations were made: 1. The usual acute hemolytic anemia which complicates sulfanilamide therapy is frequent in children (about 9 per cent of the cases) but infrequent in adults (only 3 per cent). It occurs early, within twenty-four to seventy-two hours, and reaches its maximum most often on the fifth day following the onset and almost always between the third and the seventh day. 2. The hemolysis of the red blood cells is always accompanied by (a) an abrupt rise in the icteric index (comparison of dilution color of the blood serum with a solution of potassium bichromate), (b) urobilinuria and (c) the presence of free hemoglobin in the blood. In Koletsky's case the icterus appeared on the fifth day after operation. 3. Poikilocytosis—the presence of poikilocytes in the blood (irregular red blood cells)—occurs.

In Koletsky's case the red blood cell count fell from 3,040,000 per cubic millimeter on admission to 1,600,000 on the seventh day after operation. The hemoglobin content fell from 85 per cent on admission to 38 per cent on the seventh day, while the white cells numbered 12,500 per cubic millimeter on admission and 22,200 on the seventh day.

The treatment of hemolytic anemia consists of (a) withdrawal of the drug, (b) blood transfusions, as they may possibly check the process

²²² Wood, W. B. Anemia During Sulfanilamide Therapy, *J. A. M. A.* 111: 1916-1919 (Nov. 19) 1938.

responsible for the destruction of blood, perhaps by supplying an anti-hemolytic substance, and (c) forcing of fluids

Koletsky's Case—History An elderly woman had had an infection of the upper respiratory tract and a sore throat for two weeks. Four days before her admission to the hospital, pain developed in her right ear, followed by a thin discharge from the ear.

Physical Examination She was admitted to the hospital on Jan. 10, 1939, complaining of pain in the right ear. The temperature was 101.3 F, the pulse rate, 100. The right tympanic membrane showed a perforation. There was distinct tenderness over the mastoid area. The red blood cell count was 3,600,000 per cubic millimeter, the value for hemoglobin, 85 per cent (Sahli). The Kline diagnostic and exclusion tests gave 4 plus reactions, the Wassermann reaction was negative.

A roentgenogram showed bilateral sclerosis of the mastoid bones and acute inflammation on the right side.

Treatment Simple mastoidectomy was performed on the right side. There was slight destruction of cells, many cells contained purulent exudate. Culture of the pus from the mastoid revealed the pneumococcus type III.

Sulfanilamide by oral administration was started on January 13, 1.33 Gm being given every four hours, 8 Gm on each of the next two days, and 6.7 Gm on January 16. The total dose was 24 Gm.

On January 14 (second day of sulfanilamide therapy) the red cells numbered 2,600,000 per cubic millimeter of blood, and the hemoglobin content was 65 per cent. During the next two days she complained of headache and dizziness and was disoriented.

On January 16 the temperature was 101.8 F. The red blood cell count was 1,450,000 per cubic millimeter, the value for hemoglobin, 45 per cent, and the leukocyte count, 24,300 per cubic millimeter. Sulfanilamide was discontinued. During the next two days the patient was drowsy and lethargic.

On January 17 the red blood cell count was 1,600,000 per cubic millimeter, and the value for hemoglobin, 38 per cent. A blood smear showed anisocytosis and poikilocytosis. The icteric index was 18. Liver extract was given by vein, and infusions of physiologic solution of sodium chloride and dextrose were administered.

Death occurred with the patient in coma on January 18 (eighth day in the hospital and the sixth day after institution of sulfanilamide therapy).

Autopsy The inflammation involved the tympanic antrum but not the tegmen tympani or the overlying dura. There was no leptomeningitis, and the venous sinuses of the dura contained no thrombi. The brain showed no gross or microscopic lesion.

The Kupffer cells of the liver were large and contained finely granular yellowish brown pigment, which was shown to contain iron by special stain.

Microscopically there were hyperemia and edema of the splenic pulp, which showed numerous large mononuclear cells filled with iron-containing pigment.

Microscopic section of a vertebra, of the sternum and of a rib showed a similar picture. There was distinct erythropoietic hyperplasia.

The final pathologic diagnosis was hemolytic anemia (iron pigmentation of the liver and spleen, pallor of the viscera and generalized icterus), erythropoietic hyperplasia of the bone marrow and early hypostatic bronchopneumonia.

Comment by Reviewer It seems to me that the previous treatment of syphilis had made both of these patients "allergic" to metal base drugs (see photoallergy).

Although the symptoms (outside the blood picture) were cerebral, viz., headache, dizziness and disorientation, followed later by drowsiness, lethargy and coma, they were all due, I believe, to (1) the anemia, and (2) the terminated hypostatic bronchopneumonia, as the brain and meninges at autopsy showed no microscopic change—W P E

MENINGITIS TREATED BY SULFANILAMIDE

FIRST COMPLETELY STUDIED CASES OF MENINGITIS CURED BY SULFANILAMIDE

Causse, Loiseau and Gisselbrecht,^{222a} in February 1936, reported the first recovery after treatment with a sulfanilamide derivative (the original prontosil)

Mellon and Bambas,²²³ in September 1936, successfully treated 2 patients who had streptococcic meningitis with sulfanilamide. The 2 cases appear to be the first critically studied ones on record. In the first case there was a remarkable bacteriostatic effect of the drug on the germs in the spinal fluid, manifesting itself in seventy-two hours, in the second case, this occurred in forty-eight hours. In the second case there were eight chains of streptococci per high power field and 3,000 white cells per cubic millimeter of spinal fluid. One loop of spinal fluid yielded countless numbers of colonies on a blood agar plate, yet after forty-eight hours' treatment, culture of 0.5 cc of spinal fluid gave no growth even after five days' incubation at 37 C.

SULFAPYRIDINE IN PNEUMOCOCCIC MENINGITIS

Hodes, Gimbel and Burnett²²⁴ treated 17 patients who had pneumococcic meningitis with sulfapyridine or with sulfapyridine and its sodium salt. Eight of these 17 patients (47 per cent) recovered completely. Four of the 9 who failed to survive died in less than twenty-four hours after admission to the hospital.

Doses—These authors found that sulfapyridine given by mouth is absorbed irregularly and only in limited amounts. They recommended that the use of this drug be supplemented by intravenous administration of sodium sulfapyridine at regular intervals and that the concentration of free sulfapyridine in the spinal fluid be maintained at a level of from 10 to 15 mg per hundred cubic centimeters.

222a Causse, Loiseau, and Gisselbrecht. Meningite purulente otogène à streptocoques hémolytiques, traitée exclusivement par un colorant azoïque, Guérison, *Ann d'oto-laryng*, February 1936, p 194.

223 Mellon, R R, and Bambas, L L. Bacteriostatic Effect of Sulfanilamide in Spinal Fluid of Convalescent Cases of Streptococcal Meningitis, *Proc Soc Exper Biol & Med* 36 682-683 (June) 1937.

224 Hodes, H L, Gimbel, H S, and Burnett, G W. Treatment of Pneumococcic Meningitis with Sulfapyridine and the Sodium Salt of Sulfapyridine, *J A M A* 113 1614-1619 (Oct. 28) 1939.

Toxic Effects—Toxic effects encountered from the sulfapyridine included granulocytopenia and hematuria, neither of which was fatal in any of the cases

SULFANILAMIDE AND SULFAPYRIDINE FOR STREPTOCOCCIC MENINGITIS IN CHILDREN

Silverthorne and his associates²²⁵ stated that in children sulfanilamide has reduced the mortality of streptococcic meningitis from 98 per cent to 50 per cent. Sulfanilamide had no effect in 8 cases of pneumococcic meningitis. However, 2 patients with pneumococcic meningitis recovered after the use of sulfapyridine.

The authors expressed agreement with Maclean, Rogers and Fleming that "there are still fatal cases among those treated by chemotherapy, and as it is impossible to say offhand whether the infecting pneumococcus is very sensitive to sulfapyridine or not, we suggest that to obtain the best results chemotherapy should be combined with immunotherapy."

Flake and Carey²²⁶ treated 4 children who had beta hemolytic streptococcus infection of the middle ear and mastoid complicated by meningitis with sulfanilamide and its derivatives. All recovered.

POSITIVE BLOOD CULTURES IN CASES OF PNEUMOCOCCIC MENINGITIS

Hewell and Mitchell²²⁷ collected 30 reported cases of recovery, including 3 observed by them, in which part of the treatment consisted of the use of sulfanilamide or related compounds. However, at least 8 cases of pneumococcic meningitis in which sulfanilamide was given and in which recovery did not follow have been reported. Of the 8 patients receiving sulfanilamide who died, 7 had positive blood cultures. Of the patients receiving sulfanilamide who recovered, only 1 showed pneumococci in the blood culture.

CLINICAL LESSONS FROM EXPERIMENTALLY PRODUCED STREPTOCOCCIC MENINGITIS TREATED BY SULFANILAMIDE

1. Divided doses are much more effective. In Adolph and Lockwood's²²⁸ experiments on white rats, meningitis was produced by inoculation with hemolytic streptococci.

²²⁵ Silverthorne, N., Brown, A., and Auger, W. J. Sulphanilamide and Sulphapyridine in Treatment of Disease in Children, *Canad. M. A. J.* **41**: 16-21 (July) 1939.

²²⁶ Flake, C. G., and Carey, B. W. Para-Aminobenzene-Sulfonamide and Its Derivatives in the Treatment of Beta Hemolytic Streptococcus Infections of the Middle Ear and Mastoid, *New England J. Med.* **217**: 1033-1038 (Dec. 23) 1937.

²²⁷ Hewell, B. A., and Mitchell, A. G. The Treatment of Pneumococcic Meningitis with Sulfanilamide. Review of the Literature and Report of Six Additional Cases, *J. A. M. A.* **112**: 1033-1037 (March 18) 1938.

²²⁸ Adolph, P. E., and Lockwood, J. S. Sulfanilamide in the Treatment of Experimental Streptococcal Meningitis, *Arch. Otolaryng.* **27**: 535-551 (May) 1938.

A freshly prepared 10 per cent emulsion of sulfanilamide in 16 per cent acacia was given through the stomach. The usual dose was 150 mg daily for five days. Of the animals given this amount in a single daily dose, only 25 per cent recovered, and the lives of those remaining were not definitely prolonged. However, when the same amount (150 mg) was given in two divided doses of 75 Gm each, 57 per cent of the animals survived, the average duration of life in the remainder being definitely prolonged and the clinical course of the disease altered.

2 Sulfanilamide prevents the positive blood culture. Of the untreated controls 80 per cent had positive cultures of the heart's blood, while of the treated animals that died only 1 had a positive culture. This animal died on the ninth day of the disease, four days after treatment had been discontinued.

3 Localization of bacteria is facilitated, and prevention of growth beyond the area of infiltration is induced.

Postmortem examination of the controls showed free cocci in the exudates and tissues to be much more numerous than in the treated animals. In the treated animals in which the organisms were present in considerable numbers they were either confined to a localized abscess or accompanied by a profuse infiltration of phagocytes, however, there was "no striking increase in phagocytosis."

Invasion by free cocci of tissues not yet infiltrated by the exudate was not demonstrated in any of the treated animals but was demonstrated in 63 per cent of the untreated animals. Involvement of the spinal meninges was noted in only 2 (25 per cent) of the treated animals but in 57 per cent of the untreated ones.

4 "The effect of sulfanilamide seems to be the provision of a tissue environment in which the cocci are unable to multiply freely and to invade adjacent tissues and the blood stream."

5 Intraspinal administration of sulfanilamide is not necessary in the treatment of streptococcic meningitis.

6 The drug should be given by mouth and subcutaneously.

7 It is important to employ doses sufficient to maintain an adequate level of sulfanilamide in the blood.

8 The experimental findings indicate that sulfanilamide is effective in preventing the spread of hemolytic streptococcic infections.

RECOVERIES FROM PNEUMOCOCCIC AND STREPTOCOCCIC MENINGITIS EXPERIMENTALLY
PRODUCED BY INTRACISTERNAL INFECTIONS AND TREATED BY A
SULFANILAMIDE

Kolmer²²⁹ reported experiments on rabbits and monkeys, meningitis being produced by intracisternal inoculation with virulent beta hemolytic streptococci.

²²⁹ Kolmer, I. A. Sulfanilamide in the Treatment of Experimental Streptococcic and Pneumococcic Meningitis, *Arch Otolaryng* **27** 519-534 (May) 1938.

1 Twenty per cent of the rabbits with induced streptococcal meningitis recovered. Of the untreated rabbits, all had fulminating meningitis with associated septicemia, which was fatal in eighteen to forty-eight hours, of the 46 rabbits treated with 2.5 per cent "prontosil solution" (azosulfamide) and sulfanilamide, 9 recovered, and the lives of most of those remaining were prolonged.

2 Sixty per cent of monkeys recovered. Of untreated monkeys meningitis was fatal to all in about seventy-two hours, without associated septicemia. Of 12 animals treated with sulfanilamide, administration being started twenty-four hours after the inoculation, 1 recovered.

3 Sulfanilamide has little effect on pneumococcal meningitis.

In another series of experiments on rabbits the meningitis was produced by intracisternal inoculation of pneumococci of types I, II and III, with associated septicemia, treatment with sulfanilamide did not result in recovery in any instance but definitely prolonged life in 24 of 60 animals.

In monkeys the meningitis produced by pneumococci was also associated with septicemia. Of 10 animals treated with sulfanilamide, but 1 recovered (from type III pneumococci), however, the lives of 7 others were prolonged.

In the spinal or cisternal fluids of untreated controls the streptococci were almost entirely extracellular, very numerous and in chains. In animals treated with sulfanilamide that survived the infection the cocci in the spinal fluid were rapidly reduced in number, and there was definite phagocytosis by the polymorphonuclear leukocytes, this phagocytosis was more marked in monkeys than in rabbits. No degenerative changes in the cocci were observed.

4 Kolmer concluded that the therapeutic activity of sulfanilamide in cases of streptococcal meningitis depends on the promotion of phagocytosis and that this is "probably the result of some bacteriostatic effect resulting in the production of less antiphagocytic substance."

5 Sulfanilamide is indicated in treatment of human streptococcal meningitis, and it is "worth trying" for pneumococcal meningitis.

6 Large doses should be given for the first three to five days of treatment, preferably both orally and by intramuscular injection. The oral dose should be from 2 to 12 Gm. for children (according to body weight) and 16 Gm. for adults, in twenty-four hours, given in four divided doses, the intramuscular dose when combined with oral administration should be from 10 to 50 cc. of the 0.8 per cent solution every six hours. If intraspinal injections are to be given also, the dose should be 5 to 15 cc. of the same solution for children and 20 cc. for adults every twelve hours. The dose may be reduced for patients who

respond favorably after the third to the fifth day, but oral administration should be continued for at least two to three weeks to prevent recurrence

EXPERIMENTAL MENINGITIS TREATED WITH SULFONAMIDE SALTS
MANUFACTURED IN FRANCE

Experimental Streptococcic Meningitis—During the course of his experiments, Dignonet²³⁰ used a very violent stock of hemolytic streptococci (Pion) to verify the action of this medicament and other organic sulfur derivatives on streptococcic meningitis. The infection was produced by introducing a dilution of the culture into the spinal canal by suboccipital puncture (Martin technic)

Action of Sulfanilamide—Six rabbits infected by the intraspinal route with $\frac{1}{1000}$ cc of streptococcus culture grown for twenty-two hours in bouillon serum were given 50 centigrams of sulfanilamide per kilogram of weight by mouth for three days. The controls invariably died within twenty-four hours of meningitis and streptococcic septicemia. On the other hand, in the treated animals death was delayed by more than four to five days, survival being exceptional.

Action of di-(paraaminoacetyl)-sulfone (1399 F)—Similarly, infected rabbits receiving 0.50 Gm of di-(paraaminoacetyl)-sulfone (1399 F) per kilogram of weight by mouth constantly survived for several days, during which they very often presented more or less accentuated meningeal phenomena. In this group also death was the rule.

Improved Results by Combined Action—In view of the poor experimental results, Dignonet investigated the combined action of sulfanilamide and di-(paraaminoacetyl)-sulfone (1399 F). The rabbits infected with streptococcic meningitis were given 0.25 Gm of each drug by mouth per kilogram of weight. Most of these animals recovered. However, in view of the high percentage of cures effected clinically by sulfanilamide, the advisability of applying this combined therapy to human beings appears to be debatable (Dignonet).

SULFANILAMIDE IN THE CEREBROSPINAL FLUID

According to Jauerneck and Gueffroy, sulfanilamide reaches the cerebrospinal fluid after varying intervals, in greater concentration when there is meningitis. Marshall, Emerson and Cutting noted that the

230 Dignonet, L. Traitement de la meningite streptococcique experimentale du lapin par certains derives organiques du soufre, *Compt rend Soc de biol* 130 409-411 (Feb 4) 1939, abstracted, *Neuro-Psychiatric Institute of the Hartford Retreat*, ser 7, no 69

concentration of the drug attained in the cerebrospinal fluid of the normal dog was about three quarters of that in the blood ²³¹

Concentration of Sulfanilamide in Cerebrospinal Fluid in Experimentally Produced Streptococcic Meningitis—In experiments on monkeys, Retan ²¹² found that when a hypotonic solution of sodium chloride containing sulfanilamide was given intravenously or when the sulfanilamide was given by mouth prior to intravenous injection of the hypotonic saline solution the concentration of the drug in the cerebrospinal fluid became higher than that in the blood

Passage of Sulfonamide Derivatives into the Nervous Centers—Because of the use of the sulfonamide compounds in the treatment of meningitis, Riser and Valdiguié ²³³ further investigated the exchange between blood and nervous substance by studying the distribution of sulfanilamide in the neural parenchyma

It appears that in the dog sulfonamide derivatives pass rapidly into the cerebral parenchyma and into the cerebrospinal fluid. While the latter contains only free "phenylsulfamide," the neural parenchyma contains a more or less large portion of combined sulfanilamide. The concentration in the cerebrospinal fluid and that in the brain differ. The free sulfonamide derivative is less abundant in the parenchyma than in the cerebrospinal fluid. On the contrary, the total quantity of sulfanilamide which can be liberated from the nerve tissue by hydrolysis is higher than the amount in the cerebrospinal fluid.

The molecule of *p*-aminobenzenesulfonamide (sulfanilamide), with its relatively light weight, classifies the drug with those medicaments which pass rapidly through the hematomeningoencephalic barrier.

ANALYSIS OF OTHER FACTORS IN THE EARLY CASES OF CURE

Among the early cases in which the use of sulfanilamide was included in the treatment are the following, with my analysis of the part that the factors enumerated by me played in recovery.

A case of otitic osteomyelitis in a child which developed into protective pneumococcus type III meningitis two weeks after beginning of the discharge from the ear, terminating in complete recovery, was reported by Gubner ²³⁴

231 Chemotherapy of Meningitis, editorial, *Lancet* **1** 733 (March 26) 1938

232 Retan, G. M. Intravenous Injection of Hypotonic Salt Solution Containing Sulfanilamide, *Am J Dis Child* **56** 584-593 (Sept.) 1938

233 Riser, M., and Valdiguié, P. Sur le passage des dérivés sulfamidés dans les centres nerveux, *Compt rend Soc de biol* **130** 619-621, 1939, abstracted, *Neuro-Psychiatric Institute of the Hartford Retreat*, ser. 7, no. 111

234 Gubner, J. Recovery of a Patient with Type III Pneumococcus Meningitis of Otic Origin, *Arch Otolaryng* **28** 241-251 (Aug.) 1938

A boy aged 5½ years was admitted to the hospital with pain in the right ear which had begun two weeks previously. In three days the pain had subsided, and the patient was apparently well until three days before admission, when he again complained of pain in the right ear.

On admission (Oct 9, 1937) his temperature was 103 F. There were tenderness and swelling behind the right ear and a mucopurulent discharge from the external auditory canal. The leukocyte count was 19,000 per cubic millimeter of blood, with 90 per cent polymorphonuclears. Mastoidectomy revealed pus coming through a perforated cortex. Softened bone extended forward. The tegmen antri was soft. Culture of pus from the mastoid revealed type III pneumococcus. On October 14 the patient was afebrile, and he was discharged on October 19.

On October 20 he had a frontal and occipital headache and vomited. On October 21 there developed a congested pharynx, subacute tonsillitis and an inflamed left ear. On October 24 he again complained of severe frontal headache. On the following day the temperature was 102.4 F. There was a slight puffiness over the zygoma. The Kernig sign was questionable. The deep reflexes were hyperactive. The spinal fluid was under a pressure of 32 mm of mercury, the cell count was 4,400, 100 per cent being polymorphonuclears. The culture yielded the pneumococcus type III on three occasions.

On October 25 sulfanilamide therapy was instituted, doses of 40 grains (2.6 Gm.) being given daily. Blood transfusions were also given.

On October 26 the cell count of the spinal fluid descended to 400.

On October 28 a morbilliform rash developed over the chest and shoulders, possibly due to sulfanilamide.

On October 29 the cell count was again 2,650, on October 30 it was 6,400, and then it went down again. On November 1 it was 860.

On November 2 the old wound was reopened, and the inner table over the temporosphenoid lobe was found to be necrotic. The cell count of the spinal fluid was 4,000. It subsequently went down again, but on November 8 it was again 6,250.

The diagnosis was probable osteomyelitis.

Comment by Reviewer. The sugar continued to be present in the spinal fluid, showing that the meningeal infection was at no time overpowering. And as pneumococci were not demonstrated in the fluid until October 30, which was three weeks after the beginning of the meningeal symptoms, the high cell count was indication of a good protective reaction. Pneumococci were again present on November 3 and on November 7.

In my opinion the case was one of overflow pneumococcic meningitis from a necrosing osteomyelitis of the tegmen and zygoma such as frequently occurs in young children.—W. P. E.

TOXEMIC OVERFLOW MENINGITIS

In the first case cited by Schwentker and his co-workers,²³⁵ the patient complained of earache on the right side, which subsided. The meningeal infection, I think, was an overflow from a thrombosed small

²³⁵ Schwentker, F. F., Clason, F. P., Morgan, W. A., Lindsay, J. W., and Long, P. H. The Use of Para-Amino-Benzene-Sulphonamide or Its Derivatives in the Treatment of Beta Hemolytic Streptococcal Meningitis, *Bull. John Hopkins Hosp.* 40: 297-306 (April) 1937.

vessel The cerebral symptoms—the headaches—were chiefly toxic, he was 'quite intoxicated' Cerebrospinal fluid showed very few beta hemolytic streptococci, as they were present in culture, not in smear The qualitative Benedict reaction showing reduction was present on December 6, after being absent on December 5

Comment by Reviewer The patient was cured by operation assisted by a protective reaction Sulfanilamide (10 cc of an 0.8 per cent solution given intraspinally) helped in producing a cure after the protective reaction of the fluid had been stimulated by injection of a foreign protein (meningococcus serum) —W P C

Sacks²³⁶ reported the case of a boy aged 6 years whose illness began about November 1 with a nasal discharge and a low temperature, followed by pain in the right ear and a rise in temperature The right ear drum ruptured spontaneously a week later The ear discharged for a week The temperature did not return to normal The neck became stiff, the boy was drowsy and vomited A positive Kernig sign and an equivocal Brudzinski sign were present The spinal fluid showed *Str. haemolyticus* Mastoidectomy was done on November 17

The patient had nine spinal taps, of which the first three yielded *Str. haemolyticus* He was given sulfanilamide intramuscularly and orally The spinal fluid showed a sugar content of 40.5 mg and a chloride content of 678 mg per hundred cubic centimeters The patient made an uneventful recovery

The author commented that when otitic sepsis is due to involvement of the sigmoid sinus, the primary focus being in the blood stream, the infected sinus should be incised and its contents evacuated I am of the opinion that in the presence of otitic suppurative meningitis the adjacent collection of cerebrospinal fluid should be evacuated by an incision of the dura, at least when the localized process or path of invasion is recognized

In a brief summary of the literature on hemolytic streptococcal meningitis, Kline²³⁷ referred to the recovery of more than 100 patients after use of sulfanilamide and the prontosils, as reported during 1936 and 1937

Kline cited 2 cases of hemolytic streptococcal meningitis with recovery

In the second case meningeal symptoms were present from the onset of earache, the infection probably entering directly in the line of a former fracture

On May 13 the patient, a boy, had a sore throat and pain in the right ear, and he vomited On May 16 the earache continued, the ear discharged There was stiffness of the neck and muscular rigidity On May 18 he had a fever and vomited He was restless and delirious and fell out of bed On May 19 (six days after the first aural symptom, sore throat and vomiting) he was admitted

²³⁶ Sacks, P Hemolytic Streptococcus Meningitis of Otitic Origin, *Arch Otolaryng* **28** 364-370 (Sept) 1938

²³⁷ Kline, O R Meningitis of Otitic Origin, *Arch Otolaryng* **27** 739-745 (June) 1938

to the hospital. Bacteria in the spinal fluid were so numerous at the time of operation that the prognosis was considered hopeless, however, complete recovery occurred after the use of sulfanilamide and "prontosil" (azosulfamide, disodium 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3',6'-disulfonate).

Comment by Reviewer. I am of the following opinions: 1 The overflow of virulent streptococci from the ear was controlled by sulfanilamide. 2 Many of the symptoms were those of cerebral intoxication from osteomyelitis. The toxemia of the cerebrospinal fluid was important. 3 The cerebrospinal fluid showed a plus-minus reaction for sugar, which indicated that the infection was not overpowering. 4 The pressure of the fluid was high, and the cells numbered 1,600, showing a protective reaction. The muscular rigidity at the beginning was more of toxic than of meningeal origin.—W. P. E.

CASES OF OTITIC MENINGITIS IN WHICH THE AUTHORS' STATED THE OPINION THAT OTHER FACTORS BESIDES SULFANILAMIDE PLAYED THE MAJOR PART IN RECOVERIES

APICAL DRAINAGE, THE ORIGINAL PRONTOSIL AND VITAMIN C IN THE CURE OF MENINGITIS

Langenbeck²⁴⁰ reported the complicated case of a child with bilateral otitis who had undergone several operations on both ears on account of recurrent attacks of otogenous meningitis but who finally recovered.

At one operation there was surgical destruction of the right labyrinth, so that it appeared especially important to preserve the left labyrinth and thus guard against total deafness. Meningitis developed from deeply situated foci in the petrous pyramid. Surgical intervention, first on the left ear, following the cellular system of the bone up to the end, showed a hypertrophic inflammation of the cells, with scanty pus. The right mastoid process presented inflammatory foci locally, and in view of the facial paresis there was reason to suspect that an abscess was situated in the left internal auditory meatus. After the bilateral operation the number of cells in the cerebrospinal fluid rapidly diminished under regular lumbar punctures. Postoperative healing during the first few days was assisted by regular administration of large quantities of the original prontosil (two tablets three times daily and vitamin C by mouth, because the child was undernourished). Langenbeck stated that "the normal function of the capillary plexus (of the apex) is generally assumed to be dependent on an adequate supply of vitamin C."

COMBINED ROENTGEN THERAPY AND SULFANILAMIDE IN THE TREATMENT OF OTITIC MENINGITIS

During the past two years, Woodward²⁴¹ has encountered 8 cases of meningitis, with 6 deaths and 2 recoveries. His analysis shows that sulfanilamide could hardly have been expected to influence the result.

238 Footnote deleted.

239 Footnote deleted.

240 Langenbeck, B. Operativ geheilter Fall von Meningitis ausgehend von tiefgelegenen Herden in der Felsenbeinpyramide, *Ztschr. f. Hals-, Nasen- u. Ohrenh.* **43** 354-362, 1938.

241 Woodward, F. D. Sulfanilamide and Roentgen Ray Therapy for Acute Otitis Media and Mastoiditis, *Laryngoscope* **49** 572-577 (July) 1939.

Analysis of the Deaths—The 6 deaths were due to (1) pneumococcus type XIV, (2) hemolytic streptococcus, with epidural abscess and meningitis, (3) *Str viridans*, with petrositis and meningitis, (4) *Bacillus influenzae meningitis* in a child aged 6 months, (5) hemolytic streptococcic meningitis in a child aged 2 months, and (6) pneumococcus type III, with petrositis, epidural abscess, thrombosis of the cavernous sinus, septicemia and meningitis

The conditions present on admission (*a*) were (usually) fulminating types of infection or (*b*) were due to organisms not affected by sulfanilamide and in patients whose general condition was very poor

Recoveries—There were 2 recoveries undoubtedly due to sulfanilamide. They occurred in cases of (1) infection with the pneumococcus type III, with otitis media and meningitis, and (2) hemolytic streptococcic petrositis, epidural abscess and thrombosis of the cavernous sinus

Because of the small group of cases in which the patients were treated with roentgen rays, the author has not felt that any benefit was obtained

In an analysis of all of his cases of meningitis Hall²⁴² found that there had been 7 recoveries in 21 cases. He ascertained that many of the patients had received sulfanilamide, 3 had recovered without receiving sulfanilamide, and 4 had recovered with the use of the drug, so that sulfanilamide did not seem to have made very much difference

In a case of acute labyrinthitis and meningitis reported by Hall,²⁴² the patient was completely deaf in the left ear. Lumbar puncture showed 320 cells in the cerebrospinal fluid. A Schwartze operation was performed on the left side, followed by a radical mastoidectomy and labyrinthectomy on the right ear. Sulfanilamide was given intramuscularly, together with saline solution by continuous drip. The cell count of the cerebrospinal fluid rose to 2,560 per cubic millimeter. The fluid again became turbid and contained hemolytic streptococci. It appeared as though the sulfanilamide were in complete control of the toxemia, but the bacteria responsible for the toxin were still circulating. It was thought that if a blood transfusion were given fresh antibodies might be able to deal with the organismal infection. Five days after the blood transfusion had been given the fluid was only slightly opaque and contained no organisms. The next day it was sterile and showed 6 cells per cubic millimeter.

[NOTE. Since this paper was submitted for publication, on Jan 2, 1940, I have collected more than 100 additional cases of recovery from meningitis with sulfanilamide therapy.—W P E.]

²⁴² Hall, I S. Acute Labyrinthitis and Meningitis. Recovery, *J Laryng & Otol* 54 211-213 (April) 1939

TEACHING THE LARYNGECTOMIZED PATIENT TO TALK

(WITHOUT THE AID OF THE MECHANICAL LARYNX)

NATHANIEL MARTIN LEVIN, M D

PHILADELPHIA

The problem of teaching laryngectomized patients to talk has existed since Billroth performed the first laryngectomy, in 1873. Yearly, a large number of radical extirpations of the larynx are being done, and the necessity for rehabilitation of the speech of laryngectomized patients is receiving increasing amounts of deserved attention¹. The physician's responsibility should extend beyond the operation and should provide for systematic training for recovery of natural speech.

The quality of speech depends on early training after the operation. An occasional patient stumbles into an excellent method without formal instruction. However, the principles of learning need not depend on chance, they can be directed into proper channels. The major portion of this paper will be concerned with the systematic method of training these patients to talk.

Defective speech habits and peculiar mannerisms are formed by (1) most patients who do not have the advantage of formal training in speech after laryngectomy, (2) the majority of patients who are "self taught" or who follow the example of others who have already mastered this method of speech, and (3) some patients who fail to receive sufficient elementary speech instruction owing to premature discontinuation of lessons. These patients show most or all of the following speech

Paper read and case presented before the Northern Medical Society, Philadelphia, Feb 9, 1938.

Subject presented in part in a sound motion picture in collaboration with Dr C L Jackson before the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct 9, 1939, and in the Symposium on Otorhinolaryngology, American College of Surgeons, Philadelphia, Oct 19, 1939.

1 Jackson, C, and Jackson C L. The Larynx and Its Diseases, Philadelphia, W B Saunders Company, 1937, Cancer of the Larynx, J A M A **111** 1986-1993 (Nov 26) 1938. Jackson, C L. The Voice After Direct Laryngoscopic Operations, Laryngofissure and Laryngectomy, Arch Otolaryng **31** 23-36 (Jan) 1940. Kallen, L A. Vicarious Vocal Mechanisms. Anatomy Physiology, and Development of Speech in Laryngectomized Persons, *ibid* **20** 460-503 (Oct) 1934.

defects (1) unnecessary lip movements not synchronous with speech, (2) loud blowing sounds issuing from the tracheal opening, (3) audible efforts at swallowing, which are unpleasant to the ear and obscure the speech, (4) indistinct, blurred speech, and (5) a tendency to revert to whispered speech

Forty patients taught esophageal speech may be grouped into an early, clinic series² and a larger, private series. The early group was followed from operation through convalescence until final discharge. After this, the principles of esophageal speech were taught under ideal conditions. This will be described later in detail. The later group consisted of patients who were operated on elsewhere in various clinics throughout the United States and then came to me for instruction in esophageal speech. The interval which had elapsed since they were operated on varied from four months to twelve years. None of them had received any formal speech training, some were using the mechanical larynx more or less successfully, nearly all had one or more of the aforementioned speech defects.

Since the principles of esophageal speech are dependent on the altered anatomic and physiologic status which follows laryngectomy, it may be well at this point to review a few of the more important facts. In the normal person, speech is produced by well known phenomena. A column of air strikes the vocal cords on expiration, these are set into vibration, and the vibrations are transmitted to the outgoing breath as it escapes through the closed glottis. Thus a sound is produced. Speech is then formed from this sound by the molds of speech, i. e. the tongue, teeth, lips, cheeks and palate. In the laryngectomized patient, air is swallowed or aspirated and is pocketed in the hypopharynx, in the esophagus and in the stomach. The patient then learns to expel this accumulated air past a "pseudoglottis," or vicarious larynx. This results in a vibrating column of air. Thus sound is produced by a mechanism comparable to that which acts in the normal person. Speech is produced by the molds of speech, which are unaltered after the operation.

A careful examination must be made to observe the postoperative anatomic result in each case before training is started. Equipment for this work consists of (1) a laryngeal mirror and the usual equipment of the otolaryngologist, (2) a fluoroscope or an x-ray apparatus, and (3) a kymograph, and (4) a phonograph recording machine. An examination of the nose and throat is made. The hypopharynx and the mouth of the esophagus are inspected to determine their condition after laryn-

² Chevalier Jackson Bronchoscopic Clinic, Temple University Hospital, Philadelphia, service of Dr. C. L. Jackson

gectomy and whether they are suitable for serving as an air reservoir and pseudoglottis. Use of the fluoroscope or the x-ray apparatus corroborates the findings with the laryngeal mirror and yields valuable information as to the size and location of the esophageal air pocket, the

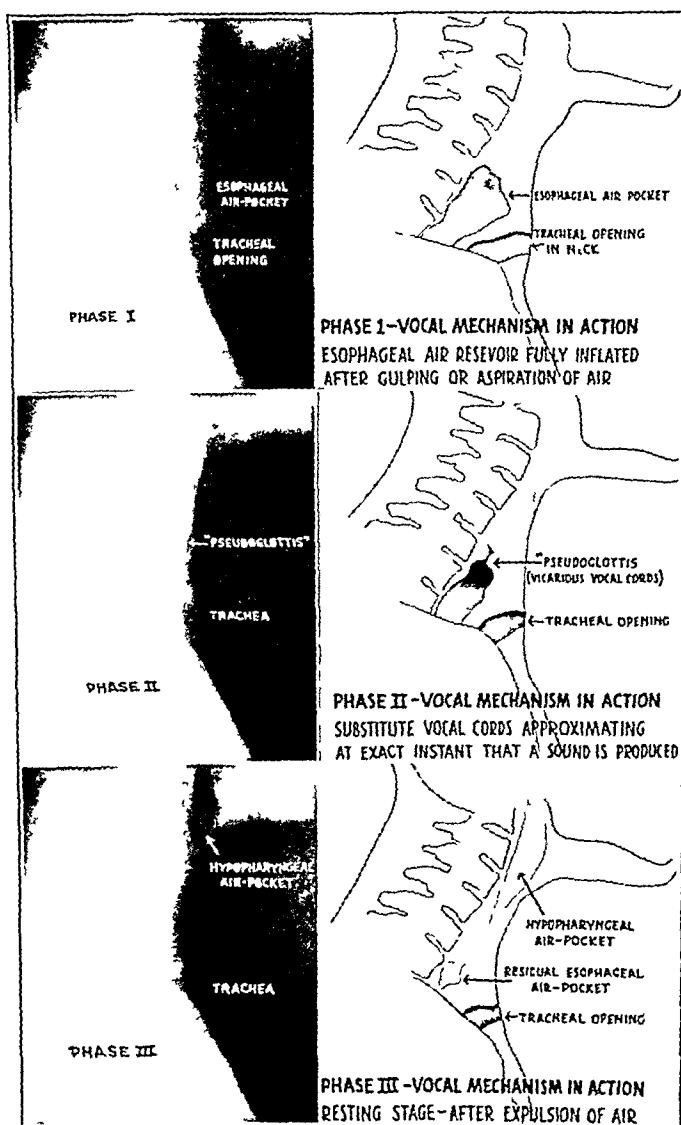


Fig 1—Roentgenograms and drawings demonstrating the three phases of esophageal speech

gastric air bubble and the nature of the pseudoglottis. The condition of the cervical musculature, the lungs and the diaphragm is observed, and the efficiency of these structures in the new vocal mechanism is determined.

It has been noted that in the beginning the laryngectomized patient is apt to overdo the act of swallowing (In these patients the gastric air bubble becomes larger and can easily be visualized fluoroscopically or by the roentgen rays) As a result, on expulsion of this accumulated air a rather loud belching sound is produced This is much more air than is necessary for production of a sound, in fact, this belching sound is unpleasant and, by its explosive character, obscures the syllable or word which is being attempted This phenomenon has given rise to an erroneous impression and to the misnomer "belch-talk" As the patient learns to control the amount of expelled air required for speech, it is found that pocketing of air occurs usually in the hypopharynx and the cervical portion of the esophagus and seldom occurs below the level of the fifth thoracic vertebra Further, as the patient develops his speech there is a migration of the air pocket from below upward As a result,

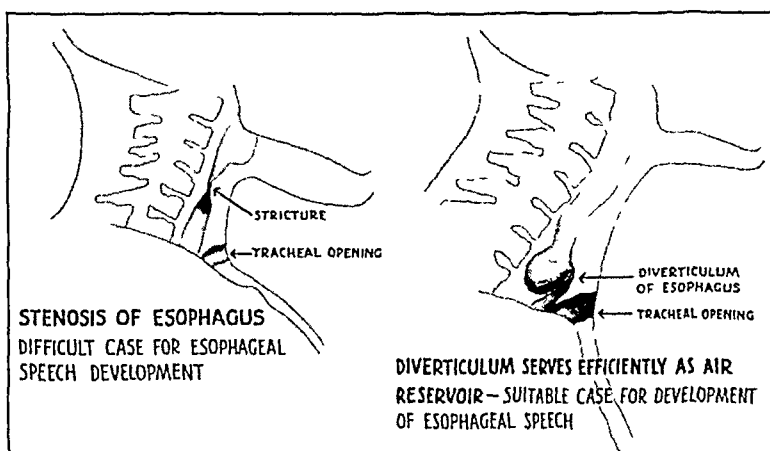


Fig 2—Contrasting conditions, one favorable and the other unfavorable to the development of esophageal speech

the swallowing, or aspiration of air and the subsequent expulsion take less time because of the shorter route Therefore the interval between syllables and words is shorter The frequently interrupted flow of words and the hesitating, halting conversation which characterize the speech of the laryngectomized patient result from the consecutive steps of this complex process

The "pseudoglottis" (vicarious larynx) varies in the individual patient, it depends on the type of operation done and on the tissues which remain after the operation The tissues which take over the function of the vocal cords as vibrators are the epiglottic tip, if this is permitted to remain, the pillars of the fauces, the tongue against the posterior wall, the collapsing esophageal wall against the opposite side,

a cicatricial band against normal tissue, a pair of cicatricial bands, and others which cannot be identified by present knowledge¹

The upper esophageal sphincter acts efficiently as a pseudoglottis if the cricopharyngeus muscle is not destroyed during the operation. This sphincter is composed of the lowermost fibers of the inferior constrictor muscle of the pharynx. It normally remains powerfully contracted and opens reflexly only during the acts of swallowing, vomiting and belching. The sphincter is supplied by esophageal ramus of the superior laryngeal nerve, and for this reason it is important to conserve as much of the nerve supply near the esophageal mouth as possible. This also has striated fibers under the control of the will and thus can act as the "vocal cords" of the pseudoglottis. During esophageal speech, air can enter the esophagus only if tonic closure of the mouth is relaxed. This action is performed by contraction of the muscles which originally tended to

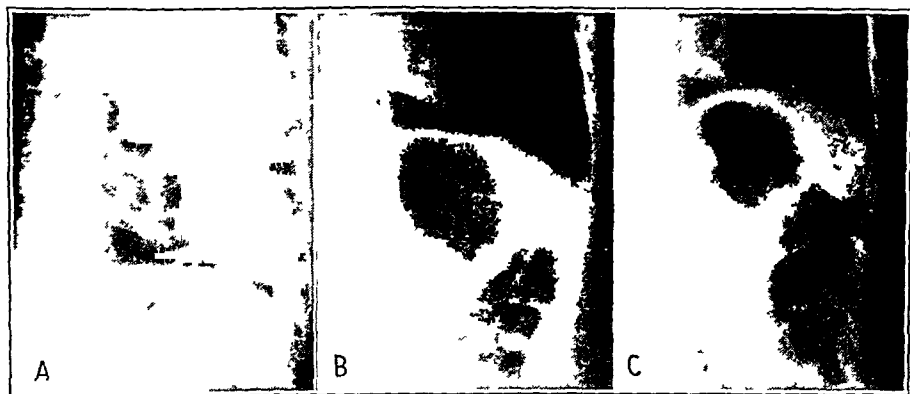


Fig 3—*A*, condition during the resting stage (before the swallowing of air) *B*, full inflation (after forceful swallowing of air). A fully inflated stomach is often noted in beginners learning esophageal speech. *C*, condition after phonation. There is only slight diminution in the size of the gas bubble, indicating that gastric air was not utilized and is unnecessary for producing a sound.

lift and pull the larynx up toward the hyoid bone, i. e., the geniohyoid and mylohyoid muscles and the anterior portion of the digastric muscles.

The sternohyoid and thyrohyoid muscles are important. Suturing these muscles to the anterior wall of the pharynx approximately at the level of the mouth of the esophagus aids in the act of aspiration. This the laryngectomized patient must learn to do efficiently and quickly at will. Soon the act becomes an involuntary reflex, and the patient no longer swallows the air but aspirates it unconsciously. Occluding the tracheal fistula with the finger increases negative pressure in the esophagus and makes it easier to aspirate air into the hypopharynx, the resulting sound is louder.

The kymograph is not essential. It is used in the phonetics laboratory for the study of respiration and the action of the thoracic cage and diaphragm.³ In addition, it is useful for recording articulation, for measuring the stream of air escaping through the mouth and nose in speaking and for determining the intensity and quality of sound.

It has been my practice to record data on beginners at the end of two weeks and again after a month to demonstrate the progress they have made. The "playback" reproduces their voices faithfully, emphasizing the good results as well as the defects.

Laryngectomy by the technic of Crowe and Broyles⁴ and, later, by that of Gabriel Tucker tends to conserve these structures very efficiently. An effort should be made during all laryngectomies to conserve as much tissue as possible in order to insure the development of esophageal speech later. Babcock^{4a} and Clerf^{4b} have made noteworthy contributions to laryngeal surgery with this in mind.

Control of the speech mechanism by the central nervous system still functions even though the lungs are no longer necessary for the act of speech. The thorax still acts as a bellows in the normal way, but on an inflated esophagus instead of on the air-filled lungs. The patient must now unlearn the basic speech habits of a lifetime and master the important dissociation of respiration through the tracheal opening and the aspiration and expulsion of air required for esophageal speech. This complex coordination of respiration, aerophagia and phonation is one of the most difficult problems encountered in training patients to master this method of speech. Also, it is at this early stage that the untrained or poorly trained patient meets considerable difficulty. Formal, systematic training is necessary to avoid speech defects.

The characteristics of esophageal speech were studied and compared with those of normal speech in a phonetics laboratory³ by spirometry and other physiologic laboratory procedures. The conclusions that may be drawn from this work are these: 1. Thoracic action for each syllable and breathing movements for phrasing are the same as those used in normal speech. 2. The normal person draws air into the esophagus with the mouth open, the laryngectomized patient learns to close the mouth and use the compressive movements of swallowing to

3 Stetson, R. H. (a) Esophageal Speech for Any Laryngectomized Patient, *Arch Otolaryng* **26** 132-142 (Aug.) 1937, (b) Speech Movements in Action, *Tr Am Laryng A* **55** 29-42, 1933.

4 Crowe, S. J., and Broyles, E. N. Carcinoma of the Larynx and Total Laryngectomy, *Ann Otol, Rhin & Laryng* **47** 875-890 (Dec.) 1938.

4a Babcock, W. W. Laryngectomy for Carcinoma of the Larynx, *S. Clin North America* **11** 1207, 1931, *A Textbook of Surgery*, Philadelphia, W. B. Saunders Company, 1939.

4b Clerf, S. H. Cancer of the Larynx, *Pennsylvania M. J.* **33** 137, 1939.

force air into the esophagus quickly 3 Three or four syllables can be said with one intake of esophageal air, or, roughly, about 1 cc of air for each syllable is required 4 The pseudoglottis must open frequently and easily for intake of air and must contract when syllables are being formed This soon becomes automatic 5 The movements of the sternum and epigastrium are more vigorous than in the normal person, therefore in the beginning, students of esophageal speech tire easily, become dizzy and have other transient symptoms

Systematic training commenced during the convalescent period will insure the proper start which is so necessary if the best results are to be obtained However, efforts to talk must not begin until the operative wound is completely healed, there are no fistulas and the patient is swallowing liquids and solids well To avoid strain on the pharynx, which is in the process of healing, all patients should be required to communicate their wishes by writing while in the hospital None should be permitted to utter any sound or even to attempt whispered speech Ambulatory patients still in the hospital because of incomplete healing of the wound, because of fistulous tracts or because catheter feedings are required have been permitted to sit in and observe a class of patients who were undergoing training This gave them their first insight into this method of speech without the aid of the mechanical larynx and served as an encouragement to them An attempt was made to have patients who talked well serve as examples to the beginners whenever possible

The class method of teaching laryngectomized patients is particularly applicable to hospitals or clinics with large laryngeal or surgical services, where a number of laryngectomized patients occupy hospital beds at the same time in progressive stages of convalescence The class method of instruction tends to conserve time Advanced pupils serve as examples and encourage those who are beginners under the direction of the instructor

An attempt was made from the very beginning to build up the morale of these patients Before operation, they received the assurance that they would talk again after the laryngectomy This assurance could be given definitely because of past experience After the operation and during early convalescence, trained laryngectomized patients were brought in to talk to these patients and to encourage them As has been stated as soon as their condition permitted, they were brought in to observe the work of the speech class They learned about the altered anatomic and physiologic status resulting from the operation They were taught the fundamentals regarding the dissociation of respiration and phonation, the latter necessitating aspiration and expulsion of air from the esophagus

The class method of instruction may be a disadvantage, in that an occasional sensitive patient may be discouraged by observing the early efforts of beginners with this method. Such a patient hears the imperfect speech of the novice and, influenced by this, becomes discouraged and leaves the class without making an effort to learn. This type is best segregated and taught individually or permitted to sit in only with trained patients. By the time local healing has occurred and the general physical condition permits, such a patient can proceed with instruction, as the fundamentals have already been acquired.

The laryngologist who undertakes the vocal reeducation of laryngectomized patients must have a fundamental knowledge of phonetics in addition to his understanding of the details of the altered anatomic and physiologic picture after this radical operation. A great deal of time and perseverance must be applied to the training of these patients if a satisfactory result is to be obtained.

The various steps employed in teaching esophageal speech are as follows

- 1 The patient begins to practice the method of swallowing or aspirating air and its subsequent expulsion. This is difficult in the beginning. Carbonated waters and effervescent solutions help somewhat in the expulsion of air. This "crutch" should not be used longer than three or four days, as the patients begin to rely on it and think themselves unable to make sounds without this aid. Also, it gives an erroneous idea of the amount of air required, as well as the false impression that the air must come from the stomach.

- 2 Easy, fundamental sounds are next to be attempted, it has been found that the fricative consonants like sh, zh, ch and sch, as found in the words church, shrub, shriek, wretch and so forth, can be produced with comparative ease. At first only one syllable can be produced with a single intake of swallowed air. Later, a sequence of syllables can be managed with the same amount of air. As soon as patients find that they can form simple words, they are much encouraged and realize that they can regain speech. Some learn this initial step immediately, others take a longer time, because they cannot grasp the fundamentals or are unable to dissociate the two now separate functions of (a) respiration and (b) phonation.

- 3 The explosive consonants are next introduced. These are found in such words as pup, dirt, top, king, gut and so forth. Vowels are attempted when the consonants are said with ease. The patients are next drilled in the various combinations of the vowels with the consonants mentioned previously.

- 4 Short words are practiced, the emphasis being placed on clarity and distinctness. At first patients are able to say only one short word.

with each cycle of intake and expulsion of air. Later, as they improve, they can say several short words with the same quantity of air. Swallowed air is then quickly converted into audible speech.

5 Longer words are next attempted. These must be broken up into their component syllables, Pensacola becomes Pen-sa-co-la. The beginner cannot say words consisting of more than one or two syllables with the same limited supply of air.

6 A series of short words are next welded into simple sentences. After each word there is a pause, and the halting speech of the beginner is apparent because of the necessity for replenishing their air supply. The initial phrases are limited to a few syllables, and the intake of air is characterized by labored interruption.

The patients are drilled thoroughly in each of the aforementioned steps. Each patient receives from thirty minutes to an hour of instruction daily and then is told to practice for thirty minute periods twice daily. Beginners may complain of dizziness, dyspnea or tachycardia, but these symptoms soon disappear.

At the end of two weeks the average patient can make nearly all the fundamental sounds, say short words and combine them into simple sentences. If the patient has no one with whom he can practice, fluency may be acquired by reading aloud. However, conversation is the best method of practicing. The expiratory blast of air issuing from the tracheal opening is still pronounced at this time, it can be minimized by blocking the opening with the finger or by teaching the patient to fix the thorax on inspiration before saying a word. This blowing sound is often very difficult to overcome. Some patients find it easier to take a breath through the tracheal opening, hold the breath, talk and then breathe out through the neck. Others breathe in and out and then talk. This constitutes a cycle which must be repeated by the beginner for each syllable. As this cycle is executed more rapidly, there is less hesitation between words and phrases, this is the beginning of fluency.

During this time patients are constantly warned against facial contortions, unnecessary lip movements and other defective speech mannerisms. They require constant encouragement. At this point a few tend to become disheartened. A continual flow of new ideas must be forthcoming to keep them interested. Although they have mastered the fundamental sounds and can make their wishes known without resorting to writing, the voice is still poor. In some the speech is marred by adventitious sounds issuing from the tracheal opening or by loud efforts at swallowing which cloud the speech. In others, the volume and carrying power are only fair, words are indistinct and articulation and diction are poor. During the next several days, considerable effort

must be directed toward eliminating these defects. If the patients are discouraged and leave at this point, their subsequent speech will probably be poor. (A number of partially trained patients have been followed up, and it was found that some had overcome their defects by themselves but that the great majority did not go beyond the point at which they discontinued formal training.)

During the next two or three weeks considerable effort is directed toward refinement of speech. All defects are eliminated as quickly as possible by constant drilling and repetition.

Whispered speech is objectionable because (1) it is toneless and ineffectual, (2) it serves as a crutch and prevents patients from learning a more desirable method, (3) it is a habit difficult to break, and (4) it is wrong from the physiologic standpoint. In whispered speech the upper esophageal pinchcock, or cricopharyngeal sphincter, must be kept tightly closed so that a sound may be produced. This is exactly opposite to what is required in esophageal speech, in which the cricopharyngeal sphincter must be trained to open quickly and easily at will.

An educated patient or one who has had training in speech or singing has a knowledge of the fundamentals and refinements of speech and language. An uneducated patient must be taught the fundamentals of phonetics and the makeup of language. Factors involved in correct speech are analyzed and applied as the patient is able to utilize what has been taught. The method for increasing the volume and carrying power of speech is taught, at first rapidity of speech is discouraged. The laryngectomized patient cannot speak as rapidly as he did before the operation. He is repeatedly told about this. Any attempt to speak with the same speed as formerly will give a very poor result. Articulation, phrasing and inflection all receive their due consideration. Other refinements are then introduced. Accent, correct pronunciation and the proper use of grammar are emphasized in training foreign patients. Enunciation and articulation, if never practiced before operation, are exceedingly difficult to acquire after laryngectomy.

Advanced training requires individual instruction. An hour is spent daily with each patient in teaching the refinements mentioned. Adequate time is necessary to master the new material presented. Talking must not be overdone, as pharyngeal fatigue occurs and may result in sore throat which incapacitates the patient for several days. Thirty minutes of practice every three hours should be sufficient at the beginning of the third week. This practice period can be increased to an hour three or four times daily if the patient's physical strength and emotional stability permit. Practice periods can be made more interesting and beneficial if they are supervised by an intelligent member of the family, a nurse or an assistant working under the direction of the laryngologist. Such

a supervisor should aim primarily at encouraging conversation and looking out for and correcting any speech defects or mannerisms as they occur

At the end of a month of instruction, the patient talks fairly well and is understood by everybody. Few, if any, speech defects remain. Efforts can now be directed toward polishing speech and preparing the patient for discharge from the speech class, he is ready for the test of talking to his friends and relatives. An occasional patient is still hesitant and somewhat timid, these fears can be dispelled by making a phonographic recording. The "playback" proves to him how well he is talking. A patient now can converse almost the entire day without fatigue. Sometimes he is apprehensive about persistent loud expiratory sounds issuing from the tracheal opening or is afraid that the carrying power of his voice has not come up to expectation. Assurance can be given that these deficiencies will be improved as he continues talking and that he may expect progressive improvement for about three years. This has been proved by follow-up recordings.

Before the student is discharged, his good points are emphasized and any residual defects brought to his attention, methods of eliminating these are given final attention. Suggestions are given as to the manner in which any monotonous quality of the voice may be overcome and a more musical quality acquired. Modulation can be improved by certain movements of the head and neck which alter the pitch of the voice. The average laryngectomized patient who has acquired this method has a range of about one octave, or about twelve halftones. A few of the more accomplished patients develop their speech to a remarkable degree of perfection.

Those of my patients who were operated on elsewhere and came later for training in speech presented peculiar and individual problems. Their difficulties existed because of the time which had elapsed since the operation, which ranged from several months to twelve years. None of these patients had received formal training in speech, and they had acquired many defects of speech in attempting to make themselves understood. Some of them were using the mechanical larynx more or less successfully.

It is my practice to work with these patients individually for one hour daily. An attempt is made to instill the fundamental principles as outlined in this paper. Usually this is difficult because of the many speech defects and mannerisms which are already ingrained from habitual use.

Another great difficulty which must be overcome is the mental attitude of these patients.⁵ The ease with which they learn is dependent

⁵ Schall, L. A. (a) *Psychology of Laryngectomized Patients*, Arch Otolaryng 28 581-584 (Oct) 1938, (b) *Laryngectomy Its Place in Treatment of Laryngeal Cancer*, Pennsylvania M J 41 261-267 (Jan) 1938

in a measure on their personalities and makeup. The aggressive extrovert goes after the problem of learning in a direct and businesslike way and acquires the method rather easily, he has the attitude of the good student. The emotionally unstable and introverted type, not having fully recovered from the psychic trauma incidental to the diagnosis of cancer and the subsequent radical operation and hospitalization, finds it difficult to concentrate and to learn anything new. Patients of this type require constant prodding, encouragement and the influence of the stronger will of the teacher. It is hard to make them toe the mark and continue with the lessons until they have acquired the method. A few of them give up the struggle easily and quit after a few days of instruction.

Necessity and willingness to learn are essential factors. This is exemplified by a patient aged 29 who was compelled to learn to talk, having the responsibility of a family and the necessity of earning a



Fig 4—Young laryngectomized patients. The man is 29 years old, the woman is 35. Such patients usually learn esophageal speech easily if they do not wait too long after the operation before beginning instruction. Their incentives are strong, they must earn a livelihood, and they are unwilling to withdraw from their social environment. These patients attack the problem of learning with vigor and determination. Patients past 60 years learn without difficulty if they have the desire to do so. However, an occasional one, with a well developed defeatist attitude, is difficult to train.

livelihood. He attacked the problem aggressively, learned readily and achieved an excellent result. In contrast, several patients to whom the necessity for earning a living was not urgent made very poor progress. A tremendous amount of patience and a great deal of time are required to teach these patients successfully.

During the last week of instruction the advanced student is encouraged to read aloud from a book. He is asked leading questions requiring lengthy replies. He may be required to tell of an incident or experience, or some interesting topic may be assigned for discussion.

He is encouraged to ramble on without any interruptions. Afterward, mistakes are noted and corrected.

Every effort is now made to improve diction, clarity and other factors which comprise finished speech. Patients are urged to practice before a mirror to detect any unconscious mannerisms and eliminate them. They are encouraged to talk to strangers and to make their wishes known in restaurants and shops or wherever the opportunity permits. Intonation is stressed and practiced constantly to make the speech more pleasant and to avoid any monotonous quality. The harshness which characterizes the early efforts at speech becomes less obvious as the patient acquires greater facility and the voice more flexibility. The best results obtained have been in those patients who began their training as early as possible after the operation, acquired the fundamentals properly and talked constantly in their occupations afterward. Among my patients I have observed many remarkable results from following this ideal program.

My experience is that women learn to talk after laryngectomy with the same ease as men. Others⁶ have stated the belief that they learn more readily.

Few patients using the artificial larynx are satisfied with this mechanical aid, all of them are anxious to discard it, even though they use it successfully. The main objections mentioned by the patients are: 1 They are conspicuous and become the objects of unwelcome attention. 2 The resulting voice is unnatural and unpleasant and has a mechanical quality. It is monotonous and does not sound human. 3 The artificial larynx serves as a constant reminder of the patient's disability. 4 The salivation caused by the instrument is unpleasant. 5 When the instrument goes out of order or is lost, the patient is helpless. 6 Use of the instrument and the successful production of speech thereby must also be learned. This requires considerable time, usually about as much as that needed to master esophageal speech.

Occasionally a patient comes with the mechanical larynx in his pocket, never having tried to master its use. A great many patients were given this mechanical aid at the time of their discharge from the hospital but were not told about the possibilities of esophageal speech. Most patients cannot use this instrument successfully without some training.

6 (a) Morrison, W. W. The Production of Voice and Speech Following Total Laryngectomy, *Arch Otolaryng* **14** 413-431 (Oct) 1931. (b) Morrison, W. W., and Fineman, S. The Production of the Pseudo-Voice After Total Laryngectomy, *Tr Am Acad Ophth* **41** 631-634, 1936. (c) Stern, H. Grundprinzipien der Sprach- und Stimmbildung bei Laryngektomierten nebst einem neuen Beitrag zum Mechanismus der Sprache und Stimme derartig Operierter, *Wien klin Wchnschr* **33** 540, 1920.

Some of them learn to speak with the artificial voice box by trial and error or by following the example of others who have acquired the method

My experience has proved that patients who use the artificial larynx readily acquire esophageal speech. One patient who used the artificial larynx very well was reluctant to meet her former friends. She discarded this appliance and mastered esophageal speech readily because of her intelligence, willingness and application. In reply to a recent follow-up letter she stated that she now talks well without the artificial larynx but uses it occasionally when engaged in a long telephone conversation, as it carries well over the telephone. Another patient finds that the mechanical larynx has more carrying power and can penetrate better above the noises of a foundry which he supervises. However, he uses his newly acquired esophageal speech in ordinary conversation. It must be remembered that these 2 patients have but recently acquired the

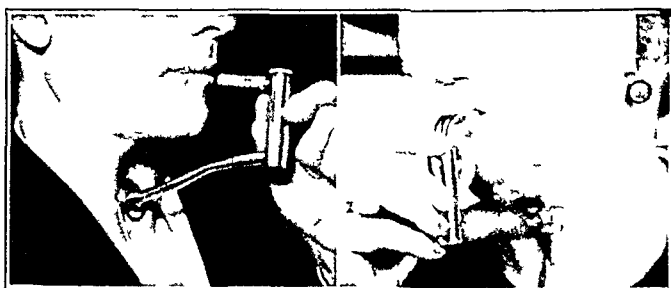


Fig 5—Use of the artificial larynx. Even when this instrument is used successfully the patients wish to discard it. The main objections are (1) it is conspicuous and (2) the resulting voice is mechanical and unnatural. (See text.)

esophageal voice, whereas they have been using the artificial larynx for a long time.

Another difficulty encountered with laryngectomized patients who wish to discard this instrument and come for instruction in esophageal speech is the fact that if they become discouraged in their early attempts at speech they can so easily fall back on this crutch. Having relied on its use for a varying period and having been able to make their elementary wishes known with it, they do not have the same incentive to learn as do those persons who have only recently been discharged after laryngectomy and cannot make themselves understood except by writing or by using the unsatisfactory whispered speech.

The artificial larynx is a distraction and a temptation to both the surgeon and the patient. It should not be tried until the patient has made every effort to develop the voice without it. No attempt should

be made to use this appliance for at least a year. It should be reserved for those few persons who cannot master esophageal speech for the following reasons:

1 Stenosis of the esophagus. In my case 1, stenosis was present as a result of partial resection necessitated by an extensive carcinoma. A patient with this condition cannot pocket sufficient air in the esophagus for the production of esophageal speech.

2 Resection of the cervical portion of the esophagus. In my case 2, the cervical portion of the esophagus as well as the larynx was removed for an extensive carcinoma. This is a definite indication for use of the artificial larynx, since the patient has no other source of air for phonation than that exhaled through the tracheal opening.

3 Other rare indications. In my case 3 the patient was totally deaf, spoke only Armenian and could not read English. Such a patient could not learn to use the artificial larynx without the greatest difficulty.

4 Suspected recurrent carcinoma. In cases of suspected recurrence of cancer, esophageal speech training should not be started. The artificial larynx may be used if desired.

In contrast to the disadvantages mentioned by those who use the mechanical larynx, the patient who has mastered esophageal speech (1) is not an object of curiosity, (2) speaks distinctly in a normal way and (3) has a voice which is serviceable and satisfactory for all normal activities. The voices of some patients are slightly husky or "throaty," being a little more harsh than the normal. However, many patients acquire a voice which is surprisingly free from any harshness and is unusually clear. Fluency of speech improves as perfection in the method is acquired. As has been stated, the quality of the voice improves steadily for about three years, as has been proved by follow-up recordings.

Trained patients have been able to pursue successfully their former occupations requiring the use of the voice, and many of them use the telephone. The majority of these persons are able to readjust themselves to their former pursuits and social environment in a most gratifying manner.

SUMMARY AND CONCLUSIONS

Since the principles of esophageal speech are dependent on the altered anatomic and physiologic status following laryngectomy, the more important characteristic anatomic and physiologic facts are reviewed.

The methods of training laryngectomized patients to talk without the aid of a mechanical larynx are discussed in detail.

The surgeon's responsibility should extend beyond the operation and should provide for systematic training for the recovery of speech.

Patients can now be reasonably assured before operation that they can learn to talk in a normal way after removal of the larynx

Speech instruction should begin as soon as healing has occurred and the physical condition permits. Esophageal speech is acquired rather easily at this time, and the development of speech defects and mannerisms is avoided.

It is urged that all laryngectomized patients first be given the opportunity to learn the esophageal method of speech, the artificial larynx should be used only as a last resort for the exceptional patient who cannot master the esophageal method.

255 South Seventeenth Street

SARCOIDOSIS OF THE LARYNX

DAVID L POE, M D

NEW YORK

This paper concerns itself in the main with a report of a case of sarcoidosis of the larynx and trachea

A diligent search of the literature failed to disclose an adequate report of involvement of those organs

Pinner,¹ in his excellent review of the literature on this subject of sarcoidosis, mentioned two reports in the foreign and one in the American literature I examined the latter It was by Longcope and Pierson² Their report was as follows "general oedema of epiglottis and laryngeal structures" That statement is of a general clinical nature, furnishing no specific information to the laryngologist It was made as the designation of a clinical finding to account for the hoarseness of a patient suffering from generalized sarcoidosis So far as I have been able to determine, the history to be given presently is the first report of sarcoid nodules in the larynx which includes a record of the results of histologic examination of the growths

Boeck's³ epochal work, published in 1899, was a study of nontender, firm, noncaseating nodules of varied sizes in the skin Boeck named the disease sarcoid because histologically the malady resembled the small cells of sarcoma Since his publication appeared, numerous clinicians have added their observations Information about this disease has accumulated disjointedly The condition has been referred to separately as a disease of the skin, of the bones, of the lymph nodes, of the uveal tract, of the parotid gland, of the tear sacs and of other parts The varied accounts, while holding to the original groundwork laid down by Boeck, have differed in particular details, and as a result several classifications have followed It is only in comparatively recent years that these clinical manifestations have been recognized as different expressions of a single pathologic process Most workers consider this disease to be tuberculous The dermatologists are perhaps best acquainted with

From the New York Post-Graduate Medical School and Hospital, Columbia University, Service of Charles M Griffith, M D

1 Pinner, M Noncaseating Tuberculosis An Analysis of the Literature, *Am Rev Tuberc* **37** 690-728, 1938

2 Longcope W T, and Pierson J W Boeck's Sarcoid (Sarcoidosis), *Bull Johns Hopkins Hosp* **60** 223-296, 1937

3 Boeck, C Multiple Benign Sarcoid of the Skin, *J Cutan & Genito-Urin Dis* **17** 543-550, 1899

it, since the majority of patients seeking the physician's aid suffer most acutely from a cutaneous lesion. Therefore, literature on dermatology carries the most numerous and perhaps the most detailed accounts. Some highly interesting studies, however, can now also be found in the literature on tuberculosis. While former reports indicated an involvement of only several organs, it is now known that all organs of the body can at one time or another be affected.

Though the disseminated sarcoid of Boeck runs a chronic course, spontaneous healing of some of the lesions may occur. In many cases the disease may last for years. It may relapse, involving one organ after another. In the meantime healing, with replacement by reduced pigment and atrophic scars of some of the lesions, may take place.

Because of the meager personal experience available to the laryngologist he is dependent on the literature for guidance in the recognition of this unfortunate disease. I shall therefore report in detail the case under observation. The paucity of the reports in the otolaryngologic literature is undoubtedly due to a lack of acquaintance with this complication.

REPORT OF A CASE

V. S., a well nourished, dark-skinned Negress 38 years of age was referred by the New York Skin and Cancer Unit to the laryngologic department of the New York Post-Graduate Medical School and Hospital, for laryngeal examination because of hoarseness lasting for the past one and a half to two years and slowly progressing.

The patient stated that before her present illness her facial features were regular, at present, the nose particularly is of the leprous type. About eighteen years ago she first observed a number of small discolorations of the skin, which disappeared in a short time. About one year afterward she had a similar attack, and the discolorations disappeared that time also. About fifteen years ago, permanent cutaneous blotches appeared, and though she has been under almost constant medical care she has shown no improvement, on the contrary, the condition has been progressive.

The history was not significant. The patient does not know of any tuberculosis in her immediate family. She is married but has not lived with her husband for a number of years and has no children.

The patient's face, nose, arms and legs and the fingers of both hands around the nails, show the characteristic nodules and plaques of Boeck sarcoid. The dermatologic ailment consists of deep blue or violet cutaneous infiltrations which have a sharply defined border and are round or oval, varying in size from that of a pinhead to a plaque of 1 to 2 cm in diameter. The infiltrations beneath the mucous membrane of the mouth and larynx have broad bases. The trunk is unaffected. Many places on the legs and arms show regression, where reduced pigmented atrophic spots or scars are located. To examining finger tips run across them, these spots give the impression of a rubbery induration not much unlike the nodules and the plaques themselves.

The alae of the nose show numerous small protruding nodules extending from the outside around the lower borders into the skin of the interior, up to but not

involving the mucosa. The skin of the anteroinferior nasal spine is also involved. Nowhere are the nodules broken down.

The mouth, pharynx, larynx and upper part of the trachea were examined, mirrors being used when necessary. The following conditions were revealed:



Boeck's sarcoid of the larynx. Beneath the epithelial covering, the stroma is made up of closely packed epithelioid cells, partly in outlined tubercles, a few of which contain giant cells of the Langhans type.

In the mouth, infiltrations have appeared in the roof recently. They are in the midline in the mucous membrane of the hard palate. The surfaces of the nodules are smooth.

The pharynx is normal.

In the larynx, the epiglottis shows numerous nodules of various sizes on the outer and the inner surface as well as on the upper border. The mucous membrane covering the nodules is thin and shiny, and broken areas are entirely absent. The right arytenoid cartilage is slightly enlarged and edematous and reveals slight nodulation. The aryepiglottic folds appear somewhat thickened, and the false cord on the left side is also thickened, but both are without evidence of nodules. The true cords are normal, with good movement during phonation as well as in respiration.

Subglottically, attached to the under surface of the true cord on the left side, an irregularly nodular mass with intact surface protrudes into the lumen of the air tube. It occupies about one fifth or perhaps one fourth of the free space of the upper part of the interior of the trachea. On the anterior and on the posterior aspect of the wind pipe, immediately below the subglottic growth just mentioned, are two fleshy masses, the posterior slightly above the anterior. They are of irregular, nodular shape and have glistening, unbroken surfaces. These masses are of such size that if they coexisted on the same level instead of steplike as they do, they would probably fill the entire lumen of the trachea.

Results of repeated Wassermann tests of the blood and von Pirquet tests, as well as tuberculin tests with old tuberculin, have always been negative.

The patient's temperature is generally normal. She suffers no pain. Her breathing is good, becoming labored only when she exerts herself physically, as in walking upstairs or in hurrying while cleaning her rooms.

This disease is chronic. It may last for years. There is no known therapy of value at the present time. Younger persons are most often affected. The literature seems to indicate that white people suffer from Boeck's sarcoid more frequently than do Negroes. One would be inclined to gather that inference from the fact that more white people suffering from the disease have been reported than Negroes. Yet arguments to the contrary can easily be advanced.

It has been stated repeatedly that the absolute diagnosis of Boeck's sarcoid is possible only by histologic examination. The general pathologist invariably makes a diagnosis of tuberculosis from a microscopic slide. A clinical description of the lesion should therefore accompany a section given to the pathologist for study.

The report on tissue taken from the epiglottis and from the subglottic masses of this patient and sent to the department of pathology of the New York Post-Graduate Medical School and Hospital of Columbia University for histologic examination was as follows:

Sections from all the tissue show the same reaction. Beneath the epithelium are tuberculoid accumulations of epithelioid cells. Within the epithelioid follicles, giant cells of the Langhans type can be seen occasionally. Necrosis and caseation are entirely absent. Polymorphonuclear cells and exudative features are also absent.

In this disease, frequently, though not always, the tuberculoid accumulations of epithelioid cells are surrounded by a thin layer of lymphocytes.

Some workers have found acid-fast bacilli in the cutaneous lesions and in the nasal secretions. The findings, however, are rare. None have ever been found in the larynx. The patient has also tuberculin anergy. The hard, nontender plaques may undergo transformation from noncaseating lesions during low anergic phases to caseating lesions during allergy.

Since sarcoidosis has come to be recognized as a peculiar type of tuberculosis it might be advisable to set down a few rules which will serve to help differentiate laryngeal sarcoidosis from laryngeal tubercles secondary to pulmonary tuberculosis.

It must be noted that in the patient reported in this paper the new growths located in the epiglottis are round circumscribed tubercles with shining, unbroken mucosa. Those below the cords are irregular, solid growths, the surfaces of which are also intact. No inflammation is visible. The true cords are completely movable. The patient does not now suffer any laryngeal pain, nor has she in the past.

In tuberculosis of the larynx secondary to pulmonary tuberculosis the lesion is most frequently located in the neighborhood of the posterior commissure or the interarytenoid space. While the anterior surface of the arytenoid body and the aryepiglottic fold may also show evidences of involvement, the incidence is far less than in the interarytenoid space or posterior commissure. When the vocal cords are affected for any time ulceration appears. Edema and congestion occur. The patient often suffers pain and other discomfort.

The roentgen findings in the chest of this patient are worthy of notation. The results of the roentgenographic examination, which was done at the roentgenologic department of the New York Post-Graduate Medical School and Hospital, were reported as follows:

Examination of the thorax shows the total heart area relatively small (the transverse diameter being fully 4.5 cm. below the average in normal persons) though of normal contour.

There are lymphomatous masses along the tracheobronchial tract, the larger and more circumscribed one of these being about 4 cm. in diameter and protruding just above and to the right of the aortic arch. There is, however, further marked increase in density, again lymphomatous, at the hilus and the root, with moderate secondary root branch and central bronchial thickening. The lesion is entirely central in origin and extent, with the peripheral lung fields comparatively clear.

Except for a moderate generalized vascularity there is no evidence of recent parenchymatous infiltration or pleural involvement.

SUMMARY

A case of sarcoid of the larynx is reported. So far as it has been possible to ascertain, this is the first complete description of Boeck's sarcoid of the larynx.

To make this report of practical value to the laryngologist, a dermatologic description of the infiltrations is also given. The roentgen findings of the chest are presented for such observations may serve as indications of deeper involvement.

Nowhere is ulceration observed. The patient experiences no pain.

745 Fifth Avenue

TREATMENT OF ACUTE LARYNGOTRACHEO-BRONCHITIS

F W DAVISON, M D

DANVILLE, PA

The clinical picture of acute laryngotracheobronchitis is so well known that I shall not discuss it. Excellent descriptions of the pathologic condition have been given by Richards¹ and others. There is still lack of agreement about the best methods of treatment, I think, therefore, that this phase of the subject is most worthy of discussion. A disease which has an average mortality of 50 per cent certainly deserves continued thought and study. During the past ten years my associates and I have treated 17 patients with this condition. Some of the data concerning these patients are given in tables 1 and 2.

There were 2 deaths in our series of 17 patients. The first occurred in 1931. A review of the record of this patient indicates that death was due to bronchial obstruction which was not diagnosed and relieved by bronchoscopic aspiration. The second death was the only one which occurred among the 10 patients treated during 1939. In this patient dyspnea developed four days before admission and death occurred five hours after admission, apparently from toxic myocarditis. Obstruction of the airway was not marked at that time.

Early recognition of this condition and admission of the patients to hospitals with adequate bronchoscopic equipment will go far to lessen the present mortality rate. Too often patients with this disease are admitted in a moribund state. A hospital admitting 10 such patients early in the course of the disease will have a much better mortality record than one which happens to admit a like number of patients who are almost exhausted, regardless of the therapeutic method used. Therefore, I believe it is pointless to compare the mortality statistics of one hospital with those of another. Moreover, I do not think that statistical study gives much indication of the efficacy of various methods of treatment, for the severity of the disease varies so greatly. This variability is dependent on two factors which cannot be accurately measured, viz (1) the virulence of the infecting organism and (2) the resistance of

From the Department of Otolaryngology and Bronchoscopy, the George F Geisinger Memorial Hospital.

Read at the Meeting of the Eastern Section of the American Laryngological, Rhinological and Otological Society, Pittsburgh, Jan 5, 1940.

¹ Richards, L. Further Study of Pathology of Acute Laryngotracheobronchitis in Children, *Ann Otol, Rhin & Laryng* **47** 326-341 (June) 1938.

the patient Two organisms may have the same appearance on the culture plates and yet differ widely in virulence If each physician will

TABLE 1—*Data on Patients with Acute Laryngotracheobronchitis Seen Before 1930*

Patient	Age	Date	Treatment	Comment	Result
1	2 yr	May 1910	Tracheotomy	Decannulation on 30th day	Recovered
2	2 yr	Sept 1911	Tracheotomy	Supraglottic edema death due to bronchial obstruction by crusts	Died
3	13 yr	March 1912	Suction through laryngoscope	Severe diabetes scarlet fever	Recovered
4	6 yr	Dec 1913	Tracheotomy	Decannulation on 6th day	Recovered
5	3 yr	Feb 1915	Late tracheotomy	Decannulation on 29th day	Recovered
6	6 yr	April 1916	Tracheotomy	Pneumonia bronchiectasis	Recovered
7	3 yr	March 1916	Suction through laryngoscope	Staphylococcal infection of 2 days' duration	Recovered

TABLE 2—*Data on Patients with Acute Laryngotracheobronchitis Seen During 1930*

Patient	Age	Date	Treatment	Comment	Result
1	18 mo	Jan 1930	Tracheotomy sulfanilamide	Decannulation on 18th day	Recovered
2	14 mo	Jan 1930	Oxygen tent sulfanilamide	Croupy cough for 2 weeks	Recovered
3	2 yr	Jan 1930	Tracheotomy sulfanilamide	Decannulation on 8th day	Recovered
4	18 mo	Feb 1930	Oxygen tent sulfanilamide	Acute follicular tonsillitis	Recovered
5	11 mo	Feb 1930	Oxygen tent	Death 5 hr after admission due to toxic myocarditis	Died
6	19 mo	March 1930	Tracheotomy sulfanilamide	Decannulation on 21st day	Recovered
7	10 mo	April 1930	Oxygen tent sulfanilamide	Rapid response to early treatment	Recovered
8	14 mo	April 1930	Transfusion sulfanilamide	Decrease in leukocyte count to 3,000	Recovered
9	18 mo	April 1930	Tracheotomy sulfanilamide	Decannulation on 5th day	Recovered
10	2 yr	Sept 1930	Suction through laryngoscope	Streptococcus	Recovered

carefully analyze his own cases in which death occurs better ways and means to lower the present mortality rate may be found Vital factors necessary for reduction of mortality are (1) early recognition of this disease by the family physician and (2) constant care in a properly equipped hospital

Treatment resolves itself into two major divisions (1) maintenance of the airway and (2) supportive treatment until the natural defense mechanism has been able to kill the invading organisms

Removal of gummy tracheal secretions and crusts by aspiration through a direct laryngoscope is certainly indicated for those patients who have obstruction due to these causes² The procedure must, of course be done by some one who has had good training and experience in direct laryngoscopy, so that instrumental trauma will not add to the subglottic edema already present

Too much reliance on suction through a laryngoscope or on intubation seems to favor the development of pneumonia for these methods allow secretions to accumulate in the bronchi A tracheotomy delayed until after the development of pneumonia will restore the airway but will not remove the pneumonia Unless the air passages are constantly kept free of secretions, pneumonia is apt to develop In none of our patients treated during 1939 did pneumonia develop, owing I think, to the fact that the airway was kept free from secretions at all times The presence of coarse rhonchi is due to thick gummy secretions which the children with this disease are unable to cough through the narrowed subglottic larynx I think that if the rhonchi persist tracheotomy is indicated to afford drainage, even though subglottic swelling is not sufficiently marked to make one feel that tracheotomy is essential to relieve the dyspnea My associates and I have not used helium and oxygen as advocated by Kernan and Barach³ Their report makes it obvious that this method is a satisfactory way of relieving dyspnea in some cases I do not think, however that it is a substitute for tracheotomy for the purpose of drainage in those patients who have much accumulated secretion in the trachea and major bronchi In almost every one of our patients requiring tracheotomy, large amounts of thick, tenacious mucus were aspirated through the bronchoscope inserted just before tracheotomy

Farber⁴ pointed out that infection in these cases spreads from above downward It is my belief that this is largely because of retention of secretions

When subglottic edema has progressed far enough to cause serious obstruction, one has the choice of intubation or tracheotomy Intubation, as pointed out by Richards⁵ Jackson and Jackson⁶ and others⁷ has

2 Tolle, D M Croup Analysis of Three Hundred and Forty-Four Cases, *Am J Dis Child* **39** 954-968 (May) 1930

3 Kernan, J D, and Barach, A L Role of Helium in Cases of Obstructive Lesions in the Trachea and Larynx *Arch Otolaryng* **26** 419 (Oct) 1937

4 Farber, S Pathologic Report in Richards⁵

5 Richards, L Fulminating Laryngo-Tracheo-Bronchitis, *Ann Otol, Rhin & Laryng* **42** 1014-1040 (Dec) 1933

6 Jackson, C, and Jackson, C L Acute Laryngotracheobronchitis, *J A M A* **107** 929-932 (Sept 19) 1936

7 Brennemann J Clifton, W M Frank, A and Holinger P Acute Laryngotracheobronchitis, *Am J Dis Child* **55** 667-695 (April) 1938

several drawbacks. Tracheobronchial secretions are apt to accumulate below the intubation tube and if not removed by bronchoscopic aspiration may well lead to development of bronchopneumonia. The presence of the intubation tube may cause pressure necrosis resulting in cicatricial stenosis of the larynx. Tracheotomy obviates both of these possibilities. A leisurely tracheotomy can be done after insertion of a 3.5 mm bronchoscope. Tracheobronchial secretions may then be removed by suction through a catheter. Should crusting occur, the crusts may be removed by means of suction tube or forceps through a 3.5 mm bronchoscope inserted through the tracheotomy fistula. One argument offered by those⁸ who advocate intubation rather than tracheotomy has been the fact that crusting tends to occur after tracheotomy because the inspired air has not been moistened by passage through the nose. My co-workers and I have been able to overcome this difficulty by the

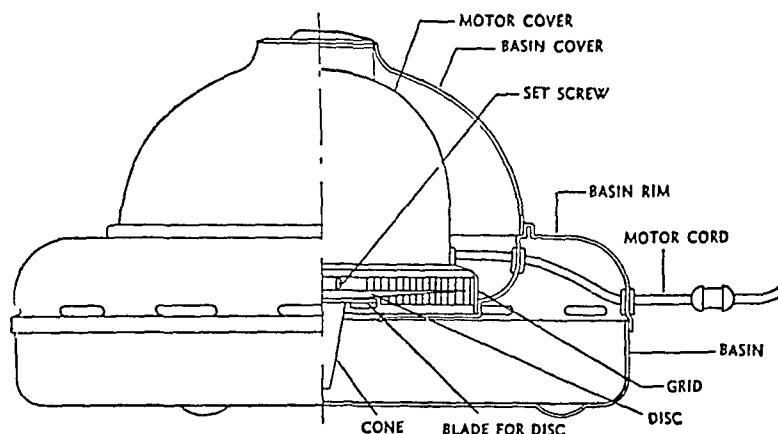


Fig 1—Diagram of cross section of the mechanical humidifier used in treatment of acute laryngotracheobronchitis

use of a well humidified oxygen tent. All authors⁹ agree that high humidity is desirable. The temperature of the air surrounding the patient is also worth considering. In the past we used a steam-humidified croup tent. This produced a temperature of 90 or 95 F and made the children uncomfortable and anxious to get out of the tent. The cool air of an oxygen tent has been advised as one means of reducing the subglottic edema occasionally resulting from the use of the broncho-

8 (a) Neffson, A. H., and Wishik, S. M. Acute Infectious Croup. A General Study of Acute Obstructive Infections of the Larynx, Trachea and Bronchi, with an Analysis of Seven Hundred and Twenty-Seven Cases, II Acute Non-Specific Infectious Croup, *J. Pediat.* **5** 617-641 (Nov.) 1934. (b) Baum, H. L. Acute Laryngotracheobronchitis, *J. A. M. A.* **91** 1097-1102 (Oct 13) 1928.

9 (a) Richards¹. (b) Brennemann and others.⁷ (c) Holinger, P. H., and Andrews, A. H. Laryngotracheobronchitis, *Southwestern Med.* **22** 174-178 (May) 1938.

scope in treating very young children. It seems reasonable to think that to employ cool moist air in treatment of this disease rather than warm moist air might tend to reduce the mucosal edema in patients with this condition, even though much of the obstruction is due to inflammatory infiltration of the conus elasticus. By the use of the humidifier¹⁰ shown in figure 1, my associates and I have been able to maintain a relative humidity of 95 per cent while the temperature of the tent remained at 68 or 70 F. We previously were able to achieve these

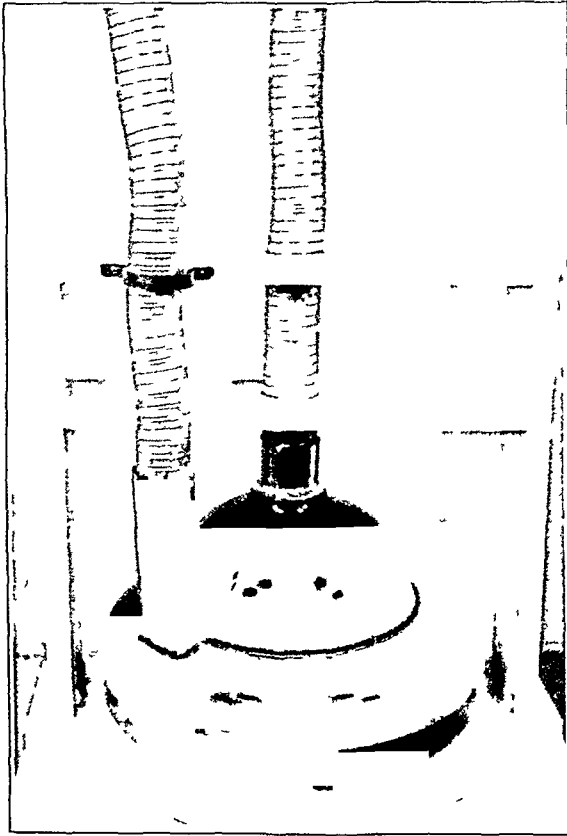


Fig 2—The humidifier modified so that it can be used to moisten the air of the canopy of an oxygen tent

atmospheric conditions by use of a steam-humidified oxygen tent driven by a motor, but this apparatus was inefficient, for the steam caused rapid melting of the ice in the ice compartment. We have adapted the mechanical humidifier as shown in figure 2 so that it has both an inflow and an outflow tube connected with the canopy of the oxygen tent. This apparatus is efficient, for it recirculates and rehumidifies the air in the tent canopy. By this means it is possible to build up quickly and to maintain a relative humidity of 95 per cent. The

¹⁰ Made by the A. C. Gilbert Co., New Haven, Conn.

temperature of the air can be varied by regulating the speed of the motor of the oxygen tent without altering the relative humidity. One can be sure of the relative humidity only by the use of a wet and dry bulb thermometer. Some of the dial type instruments for measuring humidity that are on the market at present are inaccurate and register slowly.

Instillation of a solution of sodium bicarbonate or sodium chloride through the tracheotomy tube has been advocated as a means of softening tracheal crusts which form after tracheotomy. We have not found it necessary to employ these substances since we have been using a humidified tent.

Postural drainage has been advocated¹¹ as a helpful method of treatment. The tracheobronchial secretions of the patients treated in this clinic have been so viscid that it is difficult for me to see how gravity could have much effect on the evacuation from the air passages. Introduction of staphylococcus bacteriophage through the tracheal cannula has been recommended¹² for patients with staphylococcic infection. I have had no experience with the use of this method, but it seems rational, and the cases cited bear out this point of view.

It is generally agreed¹³ that rest is an important factor in the treatment of children with acute laryngotracheobronchitis. This means, of course, that the patient should be disturbed as little and as infrequently as possible for the various examinations and treatments and in the routine nursing care. How much dyspnea is too much is a question difficult to answer, but when in doubt I have decided in favor of early tracheotomy. The children in these cases do not die as a result of a properly performed tracheotomy, but some of them certainly die if it is delayed too long. Post-tracheotomic bronchoscopy for the removal of obstructing crusts has in some instances been objected to on the ground that the patient was too sick to tolerate the procedure. Obviously a child with obstruction of the airway cannot rest, for he is using all his accessory muscles of respiration. According to the experience of my associates and myself, the use of the bronchoscope for the removal of crusts when necessary is well tolerated and produces prompt relief from the dyspnea. In the management of these children we maintain the bronchoscopic equipment in constant readiness at the patient's bedside, thus, if obstruction occurs it is necessary only to lay the child across the crib and insert a 3.5 mm bronchoscope through the tracheotomy fistula. The soft tissues around the fistula do not become infected despite repeated use of the bronchoscope. Before we learned to use a humidified tent one of our 18 month old patients

11 Galloway, T. C. Postural Treatment of Acute Laryngotracheobronchitis, *J. A. M. A.* **112** 1566-1569 (April) 1939.

12 Evans, M. G. Acute Laryngo-Tracheo-Bronchitis, *Ann. Otol., Rhin. & Laryng.* **48** 216 (March) 1939.

13 (a) Brennemann and others⁷ (b) Jackson and Jackson⁶

required 27 bronchoscopic procedures for removal of crusts. This child had no infection around the fistula and made a complete and satisfactory recovery.

A well trained special nurse must be constantly in attendance and a bronchoscopist on call day and night, in order adequately to care for the sudden emergencies that so frequently arise in these cases.

High fluid intake is another therapeutic factor emphasized by all authors¹⁴. In the experience of my associates and myself, gavage has been a satisfactory method of giving fluid, and it exhausts the patient less than the use of subcutaneous or intravenous methods. We give 10 ounces (300 cc) every four hours to 18 month old children. We believe that the child is receiving enough fluid if the specific gravity of the urine is kept below 1.015.

More about the mechanism of natural resistance to these infections needs to be known, as well as how to increase it rapidly. Specific anti-serums have been suggested, but according to Zinsser, Enders and Fothergill¹⁵ antibacterial streptococcus serums in treatment of other types of streptococcic diseases are not dependable. Recent reports¹⁶ indicate that staphylococcus antitoxic serums are effective in cases of other types of staphylococcic infections. Some means of increasing passive immunity rapidly is badly needed for children suffering with this disease.

Chemotherapy naturally suggests itself. In the cases encountered in the clinic, in which *Str. haemolyticus* was the infecting organism, the bacteriostatic effect of sulfanilamide seemed to lessen the severity and shorten the course of the disease.

Transfusion may raise the immunity rapidly by supplying non-specific complement and opsonins. We use them whenever there is severe anemia or when the clinical progress is not satisfactory.

Various drugs have been advocated for the treatment of these patients. Expectorants, such as ipecac and ammonium chloride, have been suggested. It is my belief that any slight benefit produced by such drugs is far outweighed by their tendency to cause nausea and vomiting. These, of course, are serious complications in an infant whose gastrointestinal tract is already upset by toxemia due to the infection. Since rest is such an important factor, sedatives or even narcotics might at first thought seem reasonable, yet most authors agree that the use of these substances is contraindicated¹. Restlessness is one of the outstanding signs of an hunger and should be treated by restoration of

14 (a) Richards⁵ (b) Jackson and Jackson⁶

15 Zinsser, H., Enders, J. F., and Fothergill, L. D. *Immunity, Principles and Application in Medicine and Public Health*, New York, The Macmillan Company, 1939, p. 613.

16 Baker, L. D. and Shands, A. R., Jr. *Acute Osteomyelitis with Staphylococci*. J. A. M. A. **113** 2119 (Dec. 9) 1939.

the airway rather than by administration of opiates. Atropine or belladonna may tend to dry up secretions, but by doing so it thickens them and renders their expulsion from the tracheobronchial tree more difficult.

If the maximum data concerning the bacteria in patients with this condition are to be secured, it is essential that specimens for culture be obtained from the interior of the trachea, either through a laryngoscope or through a bronchoscope. Contamination of the specimen by oral secretions will be misleading. The aspirator with collector attached shown in figure 3 is a laryngeal length modification of the Clerf aspirator. It affords a satisfactory means of clearing the trachea of secretions and at the same time provides an uncontaminated specimen for culture. Of the 10 patients treated during 1939, 9 had cultures made on blood agar plates. Of the 5 cultures made from throat swabs, 4 showed

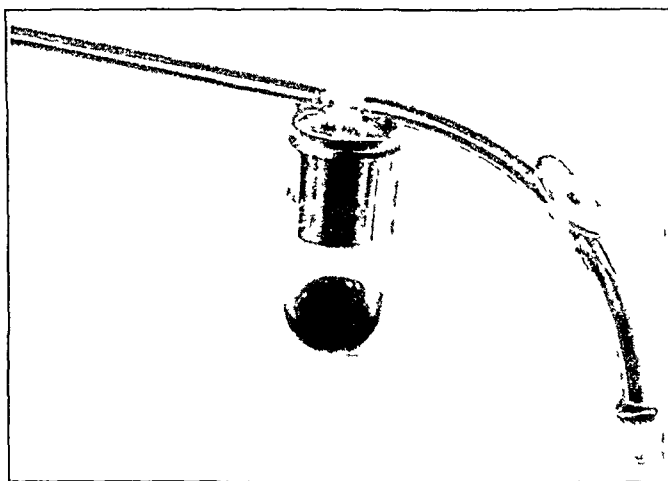


Fig. 3—Laryngeal length aspirating tube with collector attached

colonies of *Str. haemolyticus* and *Staph. albus*, while 1 showed only those of *Staph. albus*, of the 4 cultures of tracheal secretions, 3 showed a pure growth of *Str. haemolyticus* and 1 showed *Str. viridans*. Material from both throat and trachea showed no diphtheria bacilli in cultures on Loeffler's medium. It is the practice of my fellow workers and myself to use sulfanilamide routinely for these patients until the report on the culture is made on the following day and then to discontinue the use of the drug if hemolytic streptococci are not present.

The following case report will serve to illustrate some of the factors which I believe are important in treatment of this disease, and from it may possibly be deduced what each factor in treatment can be expected to accomplish.

REPORT OF A CASE

A well nourished 18 month old boy was admitted to the hospital with the chief complaint of difficulty in breathing. His symptoms began with a croupy cough only twenty-four hours before admission. The cough and dyspnea became progressively worse until the time he was admitted. The temperature had been high the night before, but on admission the temperature was only 101 F, the pulse rate 128 and the respiratory rate 22. Results of the examination of ears, nose and throat were essentially normal. The cough was croupy, and the inspiratory stridor characteristic of subglottic swelling was observed. There was only moderate inspiratory retraction of the soft tissues around the clavicles and in the epigastrium. The chest was resonant throughout, and there were no rales.

The child was placed in a steam-humidified oxygen tent and given 5 grains of sulfanilamide (0.32 Gm) every four hours. A transfusion was given because the blood count showed moderate anemia. For the first three days the patient was fairly comfortable, he took fluids well and had no toxic symptoms from the sulfanilamide. The croupy cough continued, but the temperature did not go above 101 F. On the third day for no apparent reason the temperature jumped to 103 F and the dyspnea became so marked that a tracheotomy was performed. Direct laryngoscopic examination just prior to tracheotomy showed marked swelling and induration of the subglottic tissues. It was necessary to use considerable pressure to introduce a 3.5 mm bronchoscope, a fact indicating that the swelling was due to inflammatory infiltration of the conus elasticus and not to simple edema. The tracheal mucosa was red, and the trachea contained a moderate amount of fluid mucopus. The culture from this showed a pure growth of *Str. haemolyticus*. The temperature dropped to normal the day following tracheotomy. There was no crusting, for the tracheal secretions remained fluid at all times.

Dr. Hawley's roentgenographic report after tracheotomy was as follows: "There is a great deal of moisture irregularly distributed throughout both lungs. The appearance is that of a suppurative bronchitis."

The cannula was removed without difficulty on the third postoperative day, and the child left the hospital in good condition on the eighth postoperative day.

Comment—This child was admitted early in the course of the disease. According to present standards he had the best of treatment, and yet tracheotomy was not avoided. The use of sulfanilamide and transfusions were not sufficiently effective in preventing inflammatory swelling of the conus elasticus to avoid tracheotomy. The humidified atmosphere of the tent was effective in preventing crusting after tracheotomy. At no time was it necessary to instil a sodium bicarbonate or a saline solution through the tracheal cannula. Pneumonia, septicemia or other complications did not develop, possibly because of administration of sulfanilamide.

CONCLUSIONS

Direct laryngoscopy is essential for accurate diagnosis.

Sulfanilamide is of therapeutic benefit when *Str. haemolyticus* is the infecting organism.

Subglottic edema is less marked if the patient is kept in cool moist air rather than in warm moist air.

The use of atropine and of sedatives is contraindicated in the treatment of this disease.

The development of pneumonia can usually be prevented if treatment is begun early and if the bronchi are at all times kept patent by removal of secretions and obstructing crusts.

Bronchoscopic equipment is essential for the management of patients with this disease.

Tracheotomy rather than intubation is indicated when obstructive symptoms become marked.

The mortality for this series of 17 cases was 11.7 per cent.

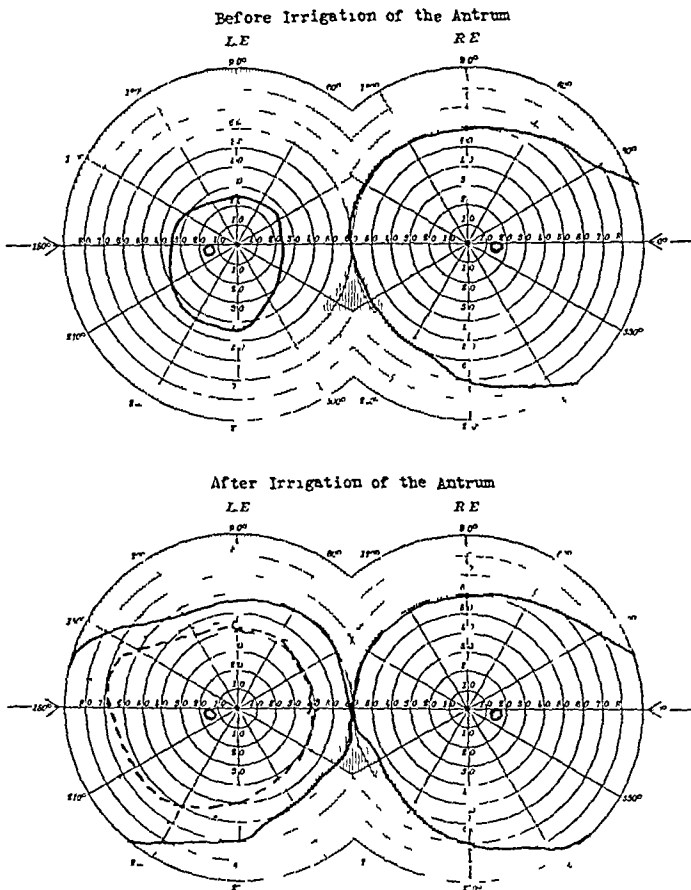
Case Reports

ACUTE ANTRITIS COMPLICATED BY OPTIC NEURITIS

E R HARCETT, M.D., AND H C ERNSTING, M.D., SPRINGFIELD, OHIO

We wish to report the following interesting case of acute antritis complicated by optic neuritis

A white girl aged 19 years was referred to one of us (H E) on Dec 14, 1939 by an optometrist She complained of hazy vision in the left eye, amounting at



The visual fields before and after irrigation of the antrum In the lower figure the broken line represents the border of the field for a blue object and the dotted line that of the field for a red object

times almost to blindness One month previously she had a cold, which caused her left cheek to become sore and painful Five days before her admission this pain and tenderness had extended to the lower margin of the left orbit, and the hazy vision had become more noticeable Ophthalmologic examination revealed a contraction in the left peripheral field, shown in the figure, and an initial refrac-

tion of 20/15 in the right eye and 20/60 in the left. The patient was wearing a plain — 50 sphere in each eye. Tenderness along the lower margin of the orbit was the only other positive finding. The optic disks were normal. The patient appeared to be emotionally stable. She was referred to the otolaryngologist.

Two days later she appeared for the otolaryngologic examination (by E. H.), stating that the condition was much worse. There was tenderness in the left canine fossa, and transillumination revealed dulness of the left antrum. The tonsils were small and not markedly inflamed. Trocar irrigation of the left antrum was immediately carried out. A small amount of light mucopurulent material was recovered. The patient returned for a check-up by the ophthalmologist three hours later, and the vision at that time was 20/15 bilaterally without correction. The visual fields were normal in form and color, as shown in the figure.

No further treatment was given, and the patient has remained well. The notable features, because of which we have reported this case, were (1) the sparsity of ocular signs other than that of the visual field, (2) the antral location of the cause, (3) the speed of recovery and (4) the simplicity of treatment.

First National Bank Building

Clinical Notes; New Instruments and Technics

DENTAL MOLDING COMPOUND CAST AND ADHESIVE STRAPPING IN RHINOPLASTIC SURGICAL PROCEDURE

GUSTAVE AUFRICHT, M D, NEW YORK

Associate Clinical Professor of Surgery, New York Post-Graduate Medical School and Hospital, Columbia University

Joseph of Berlin, father of modern nasal plastic surgery, did not use a cast after rhinoplastic operations. In fact, he was in the habit of dressing the nose with but a few thin pads of gauze gently kept in place with adhesive tapes. In order to protect the undermined and traumatized skin from necrosis through pressure, he insisted on the dressing's being light *wie ein Hauch* (as a breath).

For a number of years I employed this technic with satisfaction. There was one circumstance, though, which made me consider the application of pressure, namely, occasional hematoma formation beneath the undermined skin. Usually the hematoma was absorbed without ill effect. Sometimes, however, it proved to be a hotbed of infection. The nasal cavities can never be rendered completely aseptic, and disintegrating blood is a good culture medium for infection. In an effort to eliminate this hazard, the only solution was found in the application of pressure to prevent hematoma formation.

Cotton-roll and cork-adhesive plaster bandages, copper, lead, and other metal plate splints, Joseph's nasal clamp and similar devices have been applied for this purpose. While pressure can be provided by all, some are bulky and cumbersome and others afford partial pressure only or are too rigid or too laboriously applied. A metal plate covers the entire nose, constituting a more comfortable splint than does the cotton roll. The metal, however, does not fully adapt itself to the detailed contour of the nose. It therefore seemed to me that there was a need for a more accurately fitting and safe cast which would be easy to apply and comfortable to wear.

Searching for material, in the early part of 1927 I tried dental impression compound (Stent's mass or mold). So far as I know, no one had previously used Stent's mold for this purpose. This compound, which contains gums, waxes and resins, is hard and rigid at body temperature, becoming plastic at about 130 F (55 C). The nose was covered with a thin cast which extended to the forehead (fig 1A). To prevent cutaneous irritation through direct contact between compound and skin, a soft flannel lining was applied to the cast, which made it still gentler in its effect. The flannel also absorbed the perspiration of the skin, thus rendering the cast more comfortable for prolonged wear. The effect was highly satisfactory. Postoperative hematoma was eliminated, and infection was considerably decreased. The compound proved an ideal material for a light, easily fitting cast. Owing to its soft consistency while warm, it adapts itself exactly to the minute contour of the nose, thus assuring even pressure. If extreme edema should result, the cast is not too rigid to expand and will prevent ill effects from undue pressure.

In addition to eliminating postoperative hematoma, the cast has these additional favorable effects

1 It keeps the mobilized nasal bones and cartilages in closer approximation during the process of healing, preventing their separation by edema. This greatly increases the chances of the attainment of a narrow nose.

2 In the case of an operation for twisted or deflected nose, the cast supports the nose in the desired position during healing.

3 In cases of recent fractures of the nose, after resetting, the cast is valuable for support and for retaining the fragments in place. When pressure is needed on one side only, a half splint may be applied to the side of the nose (fig 1 *B*). In a few instances I have used narrow compound splints inside the nose to elevate the depressed fragments.

4 After operations on a saddle nose, a ring-shaped cast is often useful in keeping small transplants in place (fig 1 *C*).

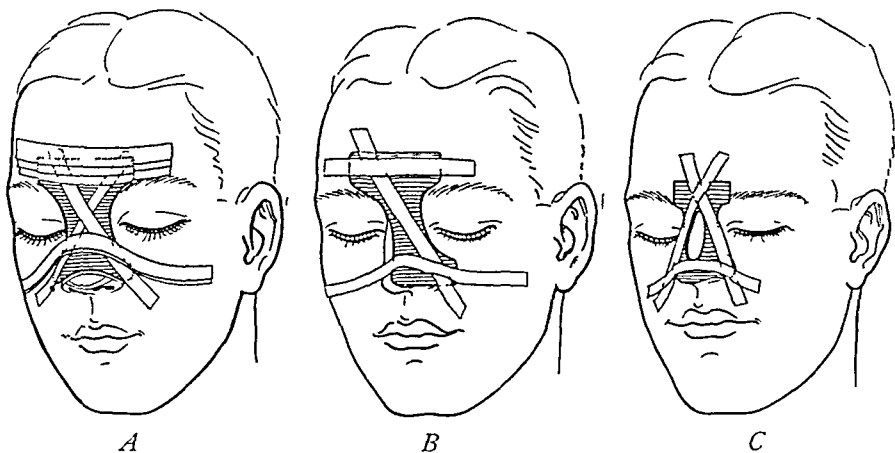


Fig 1—*A*, cast used after rhinoplastic procedure involving bone work. *B*, half cast for side pressure, as used for a fractured nose after resetting of lateral displacement. *C*, cast with a central opening for fixation of a graft in a saddle nose.

5 If traction is necessary in case of lengthening the nose, the lower edge of the cast can be extended for the fixation of traction sutures or adhesive tapes.

6 In cases of moderate depression of the cartilaginous dorsum due to retraction of the medial edges of the upper lateral cartilages, after these are severed from the septal cartilage the cast supports them in an erect position, partly above the septum, thus correcting the depression (spontaneous superposition of the upper lateral cartilages over the septum).

In addition to those advantages, the cast also provides protection during healing against trauma and against the touching or hitting of the nose during sleep.

Since 1927 I have employed this method in over 3,000 cases with full satisfaction. I have also demonstrated it to others, and I have been gratified by its wide acceptance here and abroad. In 2 cases I have observed small cutaneous lesions develop under the cast, in 1 instance on the side of the nose and in the other at the tip. In neither case did the condition appear to be due to pressure necrosis; it was caused by acne pustules which, being unable to drain, extended sideways, destroying the neighboring tissues. For the prevention of this occurrence the skin should be

carefully examined before the operation, and if there are any signs of acne or other infection the operation should be postponed until the cutaneous lesion has cleared up

TECHNIC OF APPLYING THE MOLDING COMPOUND FOR THE CAST

Before the application of the cast, it is important that no blood should be left collected in the undermined spaces. It should be gently squeezed out, especially on the sides. At this point, it may be mentioned that not only blood but also sawdust, loose bone and cartilage debris should also be carefully removed, because (1) such debris influences the shape of the nose if it collects in abundance, and (2) in case of infection it acts as foreign matter, delaying healing until it is decomposed

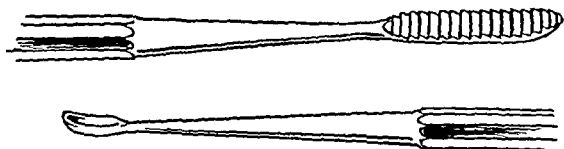


Fig 2—"Spoon" and "sweeper" for the removal of debris and sawdust

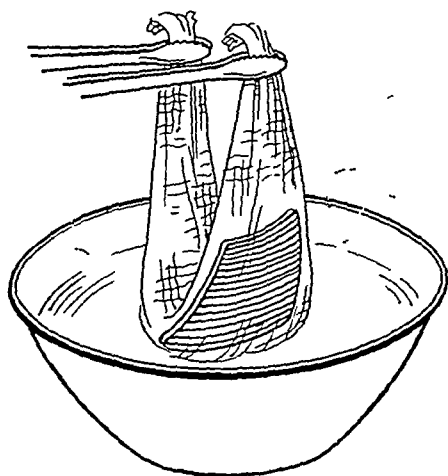


Fig 3—Immersion of Stent's mold in hot water to render it pliable

and eliminated. For the removal of debris and sawdust I use a "spoon" and "sweeper" (fig 2).

There are molding compounds which melt at higher, and some which melt at lower, temperatures. The ones with a higher melting point are preferable because they constitute a harder and lighter cast. Although it is a minor point, it is worth mentioning that red compound should be avoided since lay people sometimes mistake it for an exposed wound. The cast should be applied after the operation is completed and the nostrils are packed. Before use, the compound may be kept in a solution of mercury bichloride to sterilize its surfaces. Sterilization, however, is not absolutely necessary, since the cast does not come in contact with wounds.

The compound is furnished in plate form, one plate being usually sufficient to make a cast. Suspended in a piece of gauze, the material is immersed in water of 55 to 60 C (131 to 140 F) for twenty-five to thirty seconds, when it becomes soft and pliable (fig 3). Taken out of the gauze, it is molded and pressed over

a piece of flannel until it is not more than 2 or 3 mm thick. Lined with flannel (fig 4 *A*), the plate is trimmed to quadrangular shape, the upper end being made narrower than the base, and is placed on the nose with the flannel next to the

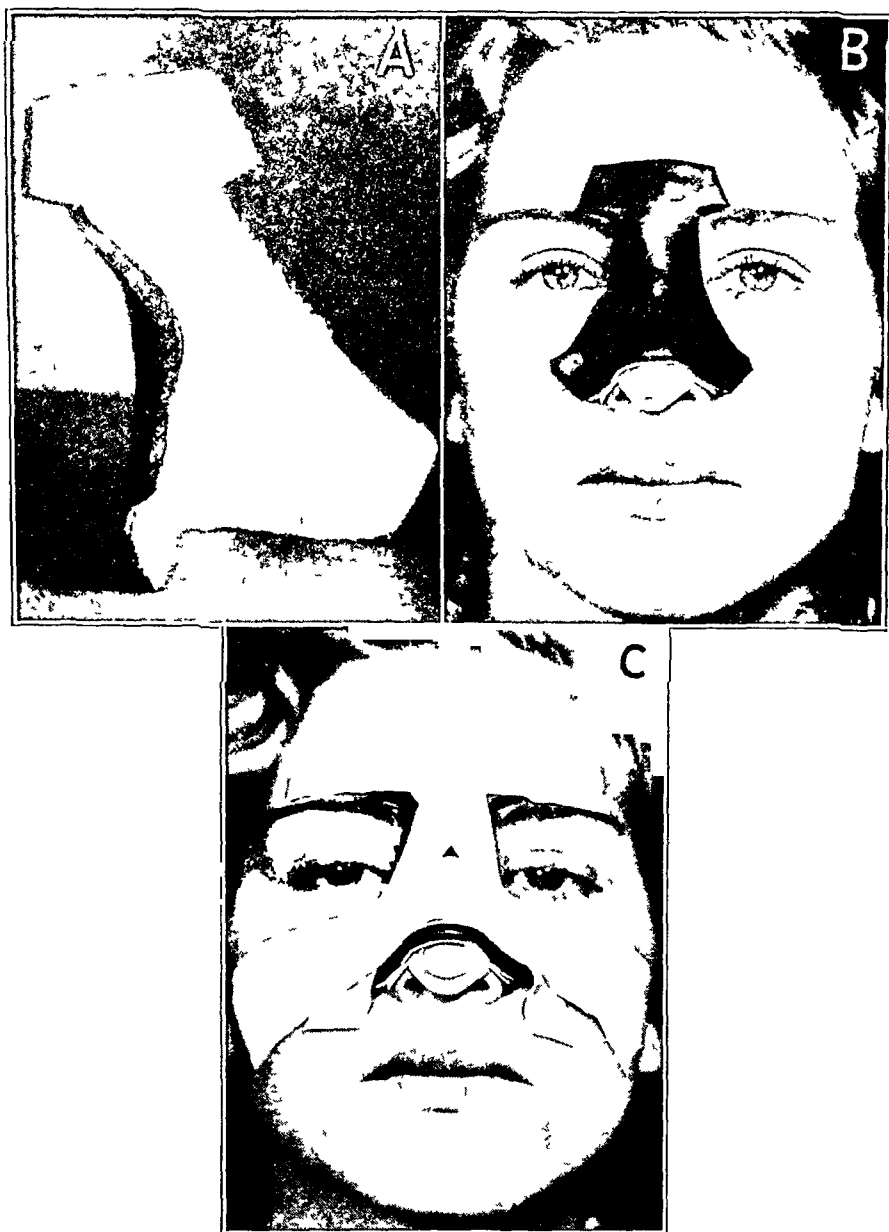


Fig 4—Photographs showing (*A*) the cast lined with flannel, (*B*) the cast in situ without adhesive tapes and (*C*) the cast held in place with adhesive tapes

skin. It covers the nose from the forehead to the tip, extending laterally to the cheeks. The sides are cut to allow clear vision and freedom of the eyelids (fig 4 *B*). The soft cast may be gently pressed against the nose with a wet, hot gauze pad to make it fit evenly. Cooled with a gauze pad soaked in ice water, it sets in a few seconds.

The cast is held in position with moderate pressure by a few adhesive tapes spread across to the cheeks and the forehead (fig 4C). A triangular piece of sterile gauze pad is attached in front of the nostrils with adhesive tape. The pad is removed after twenty-four hours. The cast remains on the nose for seven or eight days. It is not advisable to remove it either for cleaning or for checking the result. Soiled adhesive tapes may be covered with clean ones for the sake of better appearance.

Open wounds, lacerations and skin sutures often render the use of a cast, if not impossible, at least difficult. However, if they are not too extensive, provision can be made by openings on the cast for approaching and treating such areas. Otherwise the cast should be worn for only a few days instead of a week. If there is any infection or extreme irritation of the skin, the cast must naturally be removed earlier.

After the cast has been worn for a week, the skin is sometimes irritated, itchy or covered with superficial pustules. Exposure to air or the application of mild astringents or calomine lotion will clear the condition within a few days.

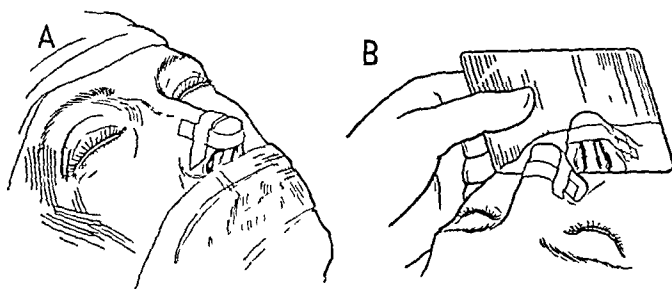


Fig 5—Drawings to illustrate the use of (A) adhesive strapping to fixate the remodeled tip and (B) a metal mirror for the control of symmetry.

ADHESIVE STRAPPING FOR THE TIP OF THE NOSE

In operations to narrow the tip of the nose, the continuity of the horseshoe-like cartilages of the tip is broken, and the crus mediale and the crus laterale become separated from each other. The free crura are suspended only by the surrounding soft tissues, so that their position becomes unstable. These small and narrow pieces of cartilage are easily separated by edema and blood or may slip into faulty position. The external effect of their separation and subluxation ranges from grooves on the skin to bulkiness, asymmetry and distortion of the tip of the nose, the alae and the nostrils.

Encouraged by the good effect which the cast had in supporting the nose, I attempted also to fixate the remodeled tip. In order to protect the loose cartilages from dislocation, I applied an adhesive loop around the tip by strapping it with two strips of adhesive tape $\frac{1}{4}$ to $\frac{1}{3}$ inch (0.6 to 0.9 cm) wide. One adhesive tape supports the tip from below, running across the under surface to the sides of the nose, while the other is laid across the tip about the height of its upper margin. Thus an adhesive loop is built about the tip, to which it gives a firm support (fig 5A). To allow the skin to shrink, the tape across the tip is lined with inverted adhesive tape $\frac{1}{2}$ to $\frac{3}{4}$ inch (1.3 to 1.9 cm) long, which prevents it from adhering to the skin.

In applying the adhesive strapping, the surgeon must be certain that the loose cartilages are in good apposition and that both halves of the tip are even. For

the control of symmetry, I employ a sterile metal mirror (fig 5B) The mirror picture at times reveals asymmetry or imperfections not noticed in a direct view Before the adhesive strapping is applied, the nostrils are gently packed with stryphnon gauze covered with petrolatum The stryphnon acts as a styptic, minimizing postoperative bleeding, while the petrolatum prevents the gauze from adhering to the wound and can easily be removed the next day The adhesive loop must not be too tight to allow for postoperative edema Otherwise the straps may cut into the skin, causing conspicuous scars Like the cast, the strapping is left on the tip of the nose for seven or eight days

103 East Eighty-Sixth Street

IMPROVED INSTRUMENTS AND POSTOPERATIVE SPLINT FOR NASAL PLASTIC OPERATIONS

Combined Chisel and Periosteal Elevator, Postoperative Nasal Splint, Forceps for Cartilage Transplants

LOUIS M. PARLMAN, M.D., NEW YORK

AN IMPROVED CHISEL

This instrument is a combination of a periosteal elevator and a chisel, joined at an angle of 65 degrees By means of this chisel the periosteum is lifted and the bone cut in one operation In addition to lifting the periosteum the elevator protects the skin from possible injury by the chisel The part of the instrument which lifts the periosteum is of sufficient thickness to make it easily felt by the fingers through the overlying skin The periosteal elevator thus serves as the guide for the direction of the chisel The acute angle formed by the chisel and the elevator engages the bone and prevents the instrument from slipping in and out

The instrument is used as follows A small incision is made in the vestibule of the nose near the lower border of the apertura piriformis The chisel is inserted through this incision, and the nasal process of the maxillary bone is engaged in the angle of the chisel The periosteal elevator is felt on its course under the periosteum with the fingers of the left hand while the chisel is guided with the right hand To cut the bony arch of the dorsum of the nose, the chisel is placed on each side of the median line and manipulated as just described Like other chisels, this chisel should be sharp and used as a cutting edge otherwise splintering of the bone occurs

The use of this chisel reduces trauma and ecchymosis and facilitates the bone work of the nasal plastic operation

AN IMPROVED POSTOPERATIVE NASAL SPLINT

A postoperative splint should meet the following requirements

- 1 It should make uniform contact with the skin covering the part operated on and adequately compress the tissues to prevent bleeding or the formation of a hematoma

From the Ear, Nose and Throat Service of the New York Polyclinic Hospital

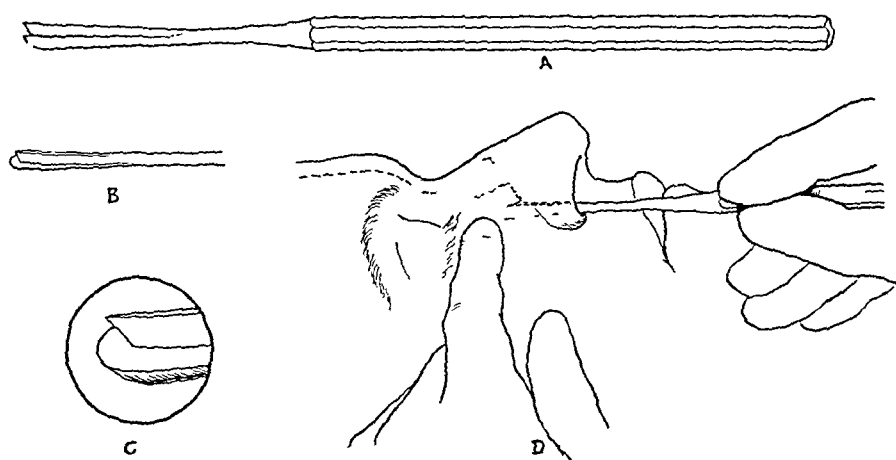


Fig 1—Combined chisel and periosteal elevator *A*, side view showing cutting edge of the chisel, periosteal elevator and acute angle for engaging the bone, *B*, anterior view, *C*, anterior view enlarged, and *D*, view showing the bone engaged in the angle of the chisel as well as the periosteal elevator felt through the skin with the index finger of the left hand while the chisel is guided with the fingers of the right hand

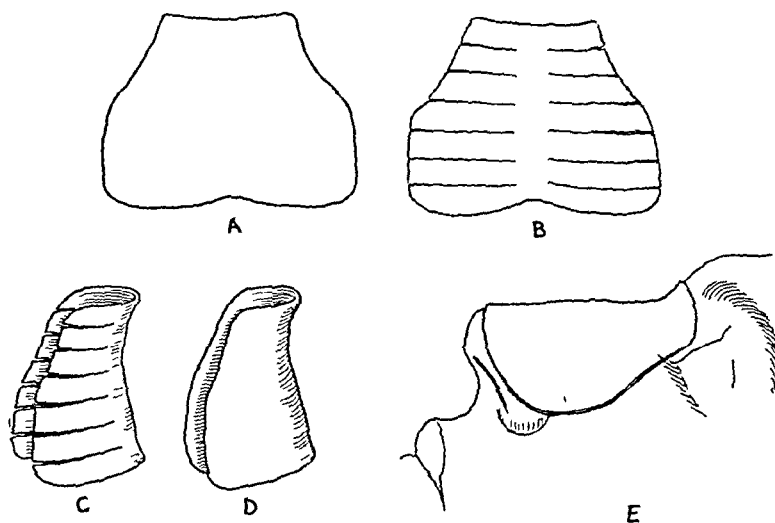


Fig 2—Improved postoperative nasal splint *A*, soft metal cut to pattern, *B*, with six cuts on each side, leaving about $\frac{1}{4}$ inch (0.6 cm) uncut in the midline, *C*, arched from above down and from side to side to approximate the form desired, *D*, completely covered with adhesive plaster on both sides, and *E*, molded to the nose

2 It must at the same time be sufficiently pliable to avoid any possibility of interference with the circulation or of injury by pressure even if excessive swelling should occur

3 It should fit snugly from the glabella to the tip of the nose, arching into the depression at the root of the nose

4 It should fit close to the eyes without interfering with the movements of the eyelids or diminishing the comfort of the patient

5 It should extend about $\frac{1}{8}$ inch (0.3 cm) beyond the line of the cut bone on each side

6 It should be smooth, light of weight and not bulky or cumbersome

These requirements are adequately met by a nasal splint made as follows. Air chamber sheet metal of medium weight (obtainable at dental supply houses) is cut after a pattern made for each individual patient. This is then cut on each side in six or eight places with a pair of shears, a line of about $\frac{1}{4}$ inch (0.64 cm) being left uncut in the middle. The splint is now arched from above down and from side to side, to the approximate form desired. It is then completely covered with adhesive plaster on both sides. The splint is molded on the nose with the

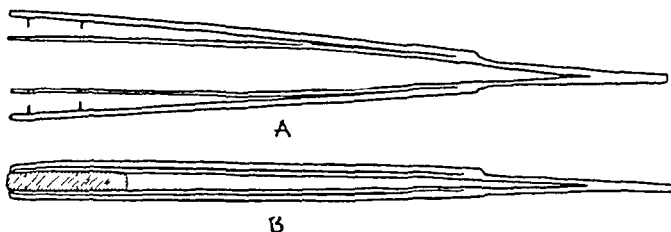


Fig 3—Forceps for cartilage transplants. *A*, view of the four-bladed forceps showing the prongs of the outer blades as well as the perforations in the inner blades, and *B*, the forceps shown with a cartilage graft in the inner blades secured by the prongs of the outer blades

fingers until every part is fitted snugly. It is then fixed with strips of adhesive plaster.

FORCEPS FOR CARTILAGE TRANSPLANTS

The unpleasant experience of having a carefully shaped cartilage graft slip away and become unfit for use in operation often results from the use of a flat-bladed forceps for manipulating the cartilage. If a toothed forceps is used, the cartilage tends to stick to one of the teeth and is usually pulled out of the undermined pocket prepared for the graft as the forceps is withdrawn.

To eliminate these difficulties a forceps has been devised which has two inner and two outer blades. Each of the outer blades has two small prongs which pass through perforations in each of the inner blades. The cartilage is held in the grasp of the inner blades and is secured by the prongs of the outer blades. When the forceps is opened, the prongs retract through the perforations of the inner blades and the cartilage is released at the desired place.

Progress in Otolaryngology

Summaries of the Bibliographic Material Available in the Field of Otolaryngology

THE PARANASAL SINUSES

SAMUEL SALINGER, M D
CHICAGO

The literature for the past year seems to indicate a more noticeable interest in diagnosis than heretofore. It is apparent that increasing knowledge of the physiology of the mucous membrane together with observations on the failure of therapy in a certain proportion of cases accounts for the desire to know more about the underlying pathogenesis of sinus disease together with the reaction of the tissues to endogenous as well as exogenous influences. Procedures which will aid in the evaluation of the degree and extent of the disease under observation are being studied with keen interest, and there is still much room for advance in this field. Planography or body section roentgenography is coming to the fore and will undoubtedly play a new and helpful role in future diagnosis.

ANATOMY AND EMBRYOLOGY

Bauermeister¹ based his studies on sagittal sections of anthropoid skulls, employing the material in the Kiel Anthropological Institute and the Museum of Lubeck, in Germany. He points out that many authors from Zuckerkandl down have shown a close relationship between the frontal sinus and the olfactory organ. Zuckerkandl, for instance, divided the sinus into two parts: (1) the pars nasalis, which in the animal is occupied by the olfactory organ, and (2) the pars frontalis, which is the true frontal sinus or hollowing out of the frontal bone. Parelli, on the other hand, failed to agree with this hypothesis, claiming that the pars nasalis is not a true pneumatic space, being merely the posterior superior portion of the regio olfactoria which is ethmoid in origin and projects forward into the nasal cavity. Bauermeister finds marked differences in the sinus architecture of various members of the monkey tribe, as follows: 1. The frontal sinus is found regularly in the chimpanzee and the gorilla, but wide variations in size may occur with differences in

¹ Bauermeister, W. Die Pneumatisierung des Schädels bei den Anthropoiden und dem Gibbon und ihre Bedeutung für die menschliche Abstammungslehre, *Ztschr f Morphol u Anthropol* 38 90 1939

age and sex. Also, there is considerable variability in the position of the sinus, so that it may communicate directly with the nasal chambers or indirectly by way of the other sinuses. 2 There is no ethmoid labyrinth in the gorilla, and the frontal sinus empties directly. 3 In the orang-utan the frontal sinus seems to develop from a prolongation of the antrum. [Vestiges of this structure may be found in man in the form of a frontomaxillary canal. S S.] 4 In the gibbon the sphenoid sinus predominates, extending far forward to communicate directly with the frontal sinus. 5 A true ethmoid labyrinth is present only in the chimpanzee. Numerous other data are presented which should be of value to students of comparative anatomy.

According to Bernfeld,² Witmaak's theory of arrested pneumatization on the basis of infantile infection is not applicable to the sinuses except, perhaps, the frontal, which develops after the infantile stage. He claims that considering the vast number of infants who suffer from colds and nasopharyngitis it is surprising that so few later in life show any evidence of arrested development of the sinuses. He cannot, therefore, subscribe to the theory that the pneumatizing power of the mucosa is amenable or sensitive to exogenous influences. As an example he cites the case of a hydrocephalic idiot with chronic maxillary sinusitis who in his eighteenth year had a well developed maxillary sinus, also, a case of congenital syphilis with infantile nasal infection in which the pneumatizing process was not hampered. The same applies to diphtheria. With regard to ozena, in which the maxillary sinuses are frequently small, with thick bony walls he presents these arguments. 1 Ozena has not been proved to be a primary infection. 2 More patients with ozena have been observed with fully developed sinuses than otherwise. 3 There are errors in interpretation of roentgen films, small sinuses having been reported because of reliance on only one projection. The author believes with Eagleton that persistence of fetal red marrow is the dominant factor in the arrest of pneumatization. The failure of red marrow to change to yellow is based on hereditary factors not fully understood but perhaps due to disturbances in the endocrine system. The author is convinced from his studies that disease of the mucosa has nothing to do with the force, speed or degree of pneumatization. [A similar study with reference to the middle ear spaces was conducted by Ruedi,³ with some interesting observations being made on the comparative roles in pneumatization played by the bone and the connective tissue as well as the mucosa. S S.]

2 Bernfeld, K. Neue Gesichtspunkte zur Pneumatisationslehre der Nasennebenhöhlen, *Pract. oto-rhino-laryng.* **2** 276, 1939.

3 Ruedi, L. Mittelohrraumentwicklung und Mittelohrentzündung, *Ztschr. f. Hals-, Nasen- u. Ohrenh.* **45** 175, 1939.

Belou's work⁴ on 23 embryos with reference to the development of the infundibulum, uncinat bone and cartilages corroborates previous studies in this connection and presents nothing new. However, the article is worth while since it is based on thorough, careful study, and the conclusions are well founded. He states that pneumatization of the nasal fossae is uniform and that extensive pneumatization of the antrums proceeds at the same rate as that of the nasal cavities. The process is limited only by early ossification of the capsule.

Van Alyea⁵ studied 100 adult specimens for grouping of cells, types of intramural encroachment as well as extramural extension, size and shape of cells and ostiums, extent of communications, direction of drainage and their clinical significance. He found frontoethmoid or supra-infundibular cells present in 53 of the specimens. Their ostium lies above the point of fusion of the bullar lamella, with the uncinat process marking the upper end of the hiatus semilunaris. The most constant infundibular cell is that which pneumatizes the agger nasi, this was found in 89 specimens. The most frequent intramural encroachment was the invasion of bullar cells by infundibular cells. This was found in 47 specimens. Extramural extension was seen in a wide variety of directions. The total number of cells averaged 9, the minimum was 4 and the maximum 17.

Cimelli⁶ sectioned 122 skulls and studied the sphenoid sinuses by the cast method. He found prolongations toward vital structures in 62 per cent of the specimens, the tendency being more frequently anterior and lateral than posterior and inferior. This would account for the frequent involvement of the optic nerve in inflammatory processes. Direct contact of the optic canal with the sinus was seen in 42 per cent of the cases. The ostium was found near the roof of the sinus in 50 per cent, halfway down in 36 per cent and near the floor in 14 per cent. Occasionally a bony septum was present which might, in the living, explain failure of drainage after surgical trephining of the sinus.

Simon⁷ is concerned with the question whether the maxillary ostium is merely an opening or a canal, since the latter is more readily occluded by inflammatory swelling. Studies of 102 antrums in cadavers revealed ostiums that were true canals 3 mm or more in length in

4 Belou, A. P. Desarrollo del seno maxilar en el embrion humano, Rev. Asoc. med. argent. **53** 37 (Jan 15) 1939.

5 Van Alyea, O. E. Ethmoid Labyrinth. Anatomic Study, with Consideration of the Clinical Significance of Its Structural Characteristics, Arch. Otolaryng. **29** 881 (June) 1939.

6 Cimelli, D. Contributo alla morfologia del seno sfenoidale, Oto-rinolaring. ital. **9** 81 (Jan) 1939.

7 Simon, E. Anatomy of the Opening of the Maxillary Sinus, Arch. Otolaryng. **29** 640 (April) 1939.

82.7 per cent of the specimens. The accessory ostiums were nearly always found to be simple openings, averaging 1.5 mm in their medio-lateral diameter.

Naatanen and Paatero⁸ studied 150 Finnish skulls and found fairly symmetric frontal sinuses extending down to the supraorbital margin, with septums in the midline in 40 per cent of the males and 26 per cent of the females. In only 1 case was there a total absence of the sinuses. The total volume of the frontal sinuses was larger in males than in females, the averages being 5.7 cc and 4.0 cc, respectively. They found that the prominence of the supraorbital ridge was usually a good index of the size of the sinus. The largest sinuses were observed in dolichocephalic and supra-brachycephalic skulls.

Roentgen studies of 1,000 heads by Stern⁹ yielded a mass of data. The maxillary sinus can be demonstrated roentgenologically by the end of the first year, develops rapidly up to the fifth year, then more slowly, reaching its maximum width in the fifteenth year and its maximum height in the fortieth year. The frontal sinus can be demonstrated in the third or fourth year and reaches its full development by the fifteenth year, although it may continue to increase in size up to the fortieth year. The author found that as a rule when the frontal sinuses were small the antrums were likewise underdeveloped, but a parallel development of frontal and ethmoid sinuses could not be demonstrated. Neither could the author show any parallel degree of pneumatization between the sinuses and the mastoids.

A similar study by Shima and Tsuji¹⁰ on 100 Japanese revealed both sinuses present in 88. The right sinus was absent in 2 and the left sinus in 4. A median sinus was present in 3. The septum was in the midline in 53 per cent, inclined to the right in 29 per cent and to the left in 17 per cent of the subjects.

Rius¹¹ refers to a case of meningitis following an intranasal ethmoid operation, reported by Mayer, in which the latter showed that the rule about keeping lateral to the middle turbinate was not infallible. The author made a number of measurements to show that it is safer to observe definite distances from the anterior nasal spine than to rely on the middle turbinate as a guide. He found that 75 mm obliquely from the spine was safe for the ethmoids and 80 mm for the sphenoid. These would represent the extreme limits beyond which surgical advance would be dangerous.

8 Naatanen, E., and Paatero, Y. Roentgenologic and Anatomic Studies on Frontal Sinuses, *Duodecim* **54** 1032, 1938.

9 Stern, L. Röntgenologische Betrachtung der Entwicklung und Ausdehnung der Nasennebenhöhlen, Hals-, Nasen- u. Ohrenarzt (pt 1) **30** 169 (May) 1939.

10 Shima, F., and Tsuji, T. Ueber die röntgenologische Untersuchung der Stirnhöhle, *J. Orient Med. (Abstr. Sect.)* **30** 162 (March) 1939.

11 Rius, M. Topografía del laberinto etmoidal para la cirugía endo-nasal, *An. de oto-rino-laring. d. Uruguay* **8** 189, 1938.

PHYSIOLOGY

Proetz and Pfingsten¹² made a study of tissue cultures for the purpose of observing reparative processes. Their contribution embraces all the details of the removal of the embryos, the preparation of blood plasma for mediums, the dissection of the animals, the preparation and care of the culture mediums, and other steps, with all the necessary precautions to avoid trauma and infection. Motion and still pictures and stained specimens record the progress of the experiments. They found that after a few hours of incubation migrating cells appeared to emerge from the tissue fragment, surrounding it in a dense zone. "Fibroblasts grow out from the implant in radiating strands and penetrate the medium for some distance before liquefaction takes place." Also the epithelial cells were observed growing out in thin strands or sheets, "the distal cells clinging to the receding wall of the medium or any debris." The authors found no difficulty in distinguishing epithelial cells from fibroblasts, as both types maintain their individual characteristics. While the data assembled were extremely interesting, the authors feel that a more extended study will have to be carried out before definite conclusions can be stated. Enough information, however, was obtained to show the natural tendency toward regeneration inherent in mucous membrane, and the first obstacle to the study has been surmounted in the stabilizing of a dependable procedure for the continued investigation of the problem.

Another piece of work, by Proetz,¹³ has to do with three parallel series of experiments for the purpose of determining the effects of drugs on the mucosa. These experiments were done on living animal mucosa undisturbed in the sinus (rabbits), on material extirpated from animals and material removed from human beings. The effects of the drugs were observed under the microscope by reflected light. The author found that the vapor of amphetamine with or without an oily base made very little impression on ciliary motility in any of the three groups. Direct application of amphetamine caused slowing of the ciliary beat to various degrees, from slowing down under a 1 per cent solution to complete cessation under a 3 per cent solution after three to six minutes. Experiments with alcohol in Locke's solution, 15 per cent, caused slowing of the rabbit's ciliary activity which was not permanent. An 18 per cent solution reduced ciliary activity at once, producing complete cessation in fifteen minutes. Activity was restored after washing in Locke's solution. A 20 per cent solution caused permanent cessation of ciliary activity. Tissues exposed to gases, such as ether and chloroform,

12 Proetz, A. W., and Pfingsten, M. Tissue Culture of Nasal Ciliated Epithelium, *Arch Otolaryng* **29** 252 (Feb) 1939

13 Proetz, A. W. Further Experiments in the Action of Drugs on the Nasal Mucosa *Arch Otolaryng* **30** 509 (Oct) 1939

suffered slowing of ciliary activity which was only temporary. Direct contact, however, resulted in permanent damage. Ether like alcohol produced cracking of the surface. The effects of chloroform directly applied were less disastrous but resulted nevertheless in permanent paralysis of ciliary activity.

By means of an ingenious machine Proetz¹⁴ was able to observe the effects of tobacco smoke on the mucosa of living animals. He shows that clinical estimations of the degree of irritation, redness and other changes are subject to such wide error as to make the conclusions inadequate. He finds the margin of error as high as 79 per cent. Even subjective signs of irritation are capable of error of interpretation running as high as 50 per cent. Some interesting observations on the objective effects of smoke delivered from a smoking machine to the nose and throat of rabbits are recorded to show the distribution of tar deposits. The author is not satisfied as yet with the results of his investigation which has only just begun. His comment that "we are still making and discarding tools" gives one an idea as to the complexity of the study. [A report on the distribution of inspired air currents within the nasal cavities by means of smoke observed through a glass model was included in last year's survey¹⁵ S. S.]

Dylewski¹⁶ is concerned with the failure of certain antrums to drain properly after operation despite seemingly adequate openings and recalls the divergence of opinion as to the proper size of these openings, quoting Hajek and Liebaute, Portman and Lautenschlager. He made a number of observations in cadavers on normal sinuses as well as on sinuses previously operated on, trying to imitate nature by producing a flow of air through the nose as in respiration and noting the effect on secretions within the sinuses. His only conclusion is that normal nasal inspiration is invaluable in helping an antrum to drain and that mouth breathing will predispose to stagnation. [The author's conclusions are not convincing because he fails to take into consideration the powerful impetus afforded by normal ciliary activity within the sinus, a factor which was absent in the cadavers. S. S.]

Van Dishoeck¹⁷ explains that with normally patent nasal passages the air currents mix freely in the nasopharynx and are distributed equally

14 Proetz, A. W. Some Preliminary Experiments in the Study of Cigarette Smoke and Its Effects upon the Respiratory Tract, *Ann. Otol., Rhin. & Laryng.* **48** 176 (March) 1939.

15 Salinger, S. The Paranasal Sinuses, *Arch. Otolaryng.* **30** 446 (Sept) 1939.

16 Dylewski, B. Investigations on the Flow of Secretions from the Maxillary Sinus, *Nowiny lek.* **51** 33 (Jan. 15) 1939.

17 van Dishoeck, H. A. E. The Course of the Inspired Air and the Possibility of Aspiration of Mucopus from One Side of the Nose into the Corresponding Lung, *Acta oto-laryng.* **27** 414, 1939.

to both lungs. By the use of carbon particles he observed that when one side of the nose is blocked the particles will tend to accumulate in the lung on the obstructed side. He demonstrated further that little nasal secretion is aspirated normally and that this mode of extension cannot be considered as a potent factor in pulmonary involvement secondary to sinus disease. However, it is possible for secretions to be aspirated during deep sleep, for Van Gelse and others have shown that secretions may pass to the piriform sinuses and overflow the incisura interarytaenoidae without exciting the cough reflex.

Parfenov's experiments¹⁸ were conducted on 77 persons in a Varocamera (a chamber in which air pressure can be regulated). He was able to produce the equivalent of ascent to 1,000 meters in one to five minutes and descent in from twenty-four seconds to six minutes. Most of his observations pertain to the effects on the ear, such as tubal obstruction and minor hemorrhages.

It is rather unusual to find an article in the German literature that shows more than a passing interest in the work of American authors. Muller¹⁹ (an exception) refers to Hilding's experiments and quotes E. King, Jates and Phillips on the topic of antrum drainage. He injected iodized sesame oil and photographed the antrums at intervals of twenty-four hours up to five or six days. He shows that in normal antrums more than half of the oil is expelled within twenty-four hours whereas in diseased antrums most of the oil is still present. In healthy antrums the oil is completely eliminated in seventy-two to ninety hours. Diseased antrums reveal oil clinging to the walls as late as six days. The author comments on the factors affecting ciliary activity including the effects of chemicals and toxic agents.

PATHOLOGY

Ertl²⁰ discusses the various theories pertaining to the constitutional factors involved in recurring nasal polypi. In a series of 40 cases he found the blood calcium low in one third and the potassium content high in two thirds. In other words, the normal proportion of calcium to potassium which is 1 to 9 was changed to 2 to 4. This alkalosis is responsible in part for the great affinity of the tissues for water, which leads to local edema. The author advises a diet rich in calcium and poor in potassium.

18 Parfenov, A. G. Effect of Reduced Atmospheric Pressure on the Ear and Sinuses, *Zhurush, nos 1 gorl bolez* 15 594, 1938.

19 Muller, E. Zur physiologischen Pathologie der Kieferhöhle, *Arch f Ohrenh* 145 248, 1938.

20 Ertl, E. Konstitutionelle Untersuchungen bei Polyposis nasi, *Monatschr f Ohrenh* 73 204 (March) 1939.

Podvinec,²¹ on the other hand believes that polypi are the result of inflammation and arise from locations in the lateral nasal wall where there is duplication of the mucous membrane such as the lips of the hiatus semilunaris, the maxillary ostium and the ostium of the individual ethmoid cells. He does not believe Hirsch's statement that they arise from within the antrum cavity proper. Numerous drawings are shown to demonstrate the acute angle formed by the margins where the mucosa lies in two layers back to back. Reference is also made to Zuckerkandl's work, which names these same locations as points of predilection for the development of polypi. The author remarks that in following polypi to their point of origin he is never able to palpate the lip or margin of the hiatus, because the polyp itself is the result of hyperplasia of this very structure, and he states further that he has never observed the pedicle of an antrum polyp to pass freely through the ostium. [Evidence to the contrary has been repeatedly reported in the literature. S S.] Thorough examination in 11 cases showed the pedicle to be attached in part to the lip of the hiatus and extending into the sinus cavity along the latter's nasal wall. In 10 cases the superior border of the hiatus was involved and in only 1 case, the inferior border. Infection, in his opinion, is secondary, and he does not believe that there is such an entity as necrosing ethmoiditis as described by Woakes. As for therapy, he is convinced that it is most important that the hiatus and infundibulum be thoroughly cleaned out.

Foulon and Desclaux²² describe a rare case, that of chloroma in a child of 22 months without the characteristic greenish cast. The symptoms were a sudden appearance of weakness in one leg and a swelling over the right eye with displacement of the bulb. The Wassermann and Kahn tests were negative. Lumbar puncture revealed slight albumin and an increase of cells in the spinal fluid. Roentgen films showed great increase in the thickness of the cranial bones, also thickening of the external layer of the right femur at the epiphysis, which resembled syphilitic periostitis. The supraorbital border was eroded. The red cells fell to 1,370,000, the hemoglobin to 55 per cent, the white cells numbered 18,800 with polymorphonuclears 53 per cent, lymphocytes 10 per cent and monocytes 27 per cent. Of the red cells, 66 per cent were nucleated. Puncture of the frontal swelling yielded mostly blood and a few abnormal cells, most of which were basophilic with few granules. The nuclear chromatin network was very delicate, without visible nucleoli, and there were frequent mitoses. Biopsy yielded friable tissue showing the same cellular elements as the puncture. Although

21 Podvinec, S. Les relations entre les polypes du nez et les affections des cavités paranasales, *Ann d'oto-laryng*, March 1939, p. 266.

22 Foulon, P, and Desclaux, P. A propos d'un cas de chlorome avant débute par des troubles paralytiques, *Sang* 13 687, 1939.

no autopsy was done, the author is certain from the roentgenograms and the results of biopsy that the disease was one of the hemopoietic medullary system. He ascribes the paresis to pressure on the rolandic area by the increased bony growth of the skull.

On the basis of 3 cases Bartelheimer²³ concludes that the frequent appearance of hyperostosis frontalis interna in hypophysial diabetes makes it an important diagnostic sign of hyperactivity of the anterior lobe of the pituitary. In 1 case he was able to relieve the severe headache by the administration of dihydrotheelin benzoate (progynon).

Gayon²⁴ discusses tissue reaction to acute infection and describes the well known histologic appearances of the sinuses in various stages of chronic disease.

DIAGNOSIS

Discussing errors in roentgen diagnosis, Schuller²⁵ first calls attention to the more common ones, such as too hard or too soft rays, asymmetric facial halves and inaccurate centering. He mentions the necessity of the horizontal projection for demonstrating fluid level, also the need for a sufficient number of axial and tangential projections for the posterior ethmoid and sphenoid sinuses. The more angles of projection the less danger there is of overlooking variables in the size and shape of individual sinuses or of missing recesses of the frontal, maxillary and sphenoid sinuses. The author further stresses the importance of studying the bony walls of the sinuses as closely as is the custom with the mastoid. Clues may often be found which are helpful in determining the severity and extent of the lesion. Thickened sinus walls may be present long after sinus symptoms have subsided. "Persinusitis ossificans," in which the walls have become thickened by new bone formation, may be the cause of persisting headaches, visual disturbances and other symptoms without any local findings in the nose or sinuses.

Johnson²⁶ made an analysis of the results from 854 successive roentgen examinations of the sinuses in cases in which the clinical records were complete, in order to determine their value in diagnosis. His routine projections are the Waters, Rhese, verticomental and lateral. The Waters and Rhese projections are always stereoscopic. A comparison of the roentgen with the clinical diagnosis shows a close parallel, the former being positive in 632 cases and the latter in 614. Agreement

23 Bartelheimer, H. Die Hyperostosis frontalis interna als Symptom des hypophysären Diabetes, *Deutsche med. Wchnschr.* **65** 1129 (July 14) 1939.

24 Gayon, P. J. Histopathology of Sinusitis, *South M. J.* **32** 211 (Feb.) 1939.

25 Schüller, A. Fehlerquellen der Röntgendiagnose von Nebenhöhlenaffektionen, *Acta oto-laryng.* **27** 159, 1939.

26 Johnson, V. C. The Value of Roentgen Examination of the Paranasal Sinuses, *Radiology* **32** 303 (March) 1939.

between the two was positive in 539 and negative in 140, a total of 679, or 80 per cent of the entire group. Of 133 cases in which operation was done, disease was proved present in 131. The clinical and roentgen diagnoses were in agreement in 128 of these. "Clouding" merely means loss of air content. It is often difficult to say whether it is due to excessive swelling of the mucosa, to neoplasm or to accumulation of fluid. An analysis of the findings in 163 sinuses which were operated on and in which simple clouding was reported through preoperative roentgen study reveals that the most frequent findings were pus, in 63, and pus and thickened membrane, in 67. In 37 sinuses operated on in instances in which the preoperative roentgen diagnosis was "thickened membrane" the findings were pus, in 13, and pus and thickened membrane, in 15. "Clouding with bone involvement," reported in 13, proved to be malignant tumor in 6 and osteomyelitis in 6. "Expansion" of a sinus usually means tumor. In 11 sinuses operated on for this condition the preoperative roentgen findings were confirmed. In several cases in which osteitis was not recognized in the roentgen examination, this process was found at operation, the diagnosis having been missed because the location of the disease was such that the area was inaccessible to clear interpretation on account of the overlapping shadows. The changes were mainly in the ethmoid area.

Casati²⁷ describes a machine for stratigraphy, made by the firm of Meschia-Metaliz, which may be used for both the Vallebona and the Borzetti technique. The article is full of technical details and is illustrated by a number of projections of the skull at various depths, in which the author points out the various details of sinus topography and the landmarks of the skull as they come into view at different levels.

Seuntjens²⁸ also presents a diagram showing how tomography works, with a few illustrative pictures of normal ethmoid and sphenoid sinuses. He states that another paper is forthcoming on the use of this procedure in diagnosis of diseased sinuses.

Weve and Ziedses des Plantes²⁹ report a case of optic atrophy and paresis of the extraocular muscles due to an isolated lesion in the ethmoid bone which was not seen in the routine roentgen films but which showed up beautifully in the planographic studies at a depth of 5 cm. [A similar report by Dean, Moore and Cone before the American

27 Casati, A. La stratigrafia dei seni della faccia, *Radiol med* **26** 546 (June) 1939.

28 Seuntjens, H. Tomographies des sinus paranasaux chez le normal, *Bull Soc belge d'otol, rhin, laryng*, 1939, p. 54.

29 Weve, H., and Ziedses des Plantes, G. B. Planigraphischer Nachweis einer Nebenhöhlen-verschleierung mit orbitalen Komplikationen, *Ophthalmologica* **97** 346 (Aug.) 1939.

Laryngological Association will undoubtedly soon appear in print. Incidentally, these authors suggest the term "body section roentgenography" as more descriptive than "tomography" "stratigraphy" and "planography" S S]

Thienpont³⁰ states that allergy must influence the interpretation of roentgen films. When the routine roentgen and clinical examinations are inconclusive, he advises studies with iodized poppyseed oil plus a determination of the emptying time. Ciliary activity in the sinuses remains almost normal despite extensive polyposis of allergic origin, whereas it is markedly impeded if the pathologic condition is truly infective. Cases are cited to prove this point.

Weill³¹ claims that he can outline the limits of the frontal sinus under transillumination by pressure with the thumb parallel to the brow, starting just below the hair line and descending slowly until the shadow suddenly becomes clear. The same procedure is done from without inward. Compression of the soft tissues permits sharper definition of light and shadow between the pneumatic and the solid bone.

Hargett³² recommends pulling the lower lid down in order to observe the crescentic light in the alveolar tissue below the bulb when transilluminating the antrum. [This method was reported by Delobel³³ as a point in differentiating between osteoperiostitis of the superior maxilla and maxillary sinusitis, both of which give a dark antrum when viewed through the cheek, the light crescent, however, would be absent in the case of sinusitis and present if it were a case of osteoperiostitis S S]

De Lima³⁴ claims to be able to fill the sinuses with contrast medium by having the patient try to inhale forcibly while in the Parkinson position with the nares pinched off. The negative pressure induced after four or five attempts will displace the air and permit the fluid to occupy the sinus spaces.

Tato³⁵ describes displacement in the Parkinson position and shows some roentgen pictures illustrating typical cases.

30 Thienpont, R. Le radio-diagnostic des affections allergiques du nez et des sinus, Bull Soc belge d'otol, rhin, laryng, 1939, p 32

31 Weill, G A. Diaphonoscopia des sinus frontaux, Oto-rhino-laryng internat **23** 63 (Feb) 1939

32 Hargett, E R. An Aid to Interpreting Transillumination of the Antrums, Arch Otolaryng **29** 985 (June) 1939

33 Delobel, P. L'osteoperiostite du maxillaire superieur, cause d'erreur dans la diaphonoscopia et la radiographie, Echo med du Nord **5** 273 (Feb 16) 1936

34 de Lima, E. Variante de la methode de Proetz, Ann d'oto-laryng, October 1938, p 929

35 Tato, J M. El metodo de desplazamiento de Proetz para el diagnostico y tratamiento de las sinusopatias nasales, Rev Asoc med argent **53** 725 (Aug 15-30) 1939

Seuntjens³⁶ believes that the examination of aspirated fluid from the sinuses, introduced by displacement, will offer data that will be helpful in diagnosis of obscure lesions, particularly when disease of the ethmoid sinuses is suspected. He uses a stated quantity of saline solution (200 cc) and makes a cell count of the aspirated fluid. By comparison with tables prepared from observations made on a number of normal persons he claims to be able to show that an increase in the number of cells and in the percentage of albumin points strongly to a diseased focus.

Metz³⁷ believes that by measuring pressure changes within the antrum via a puncture needle attached to a suitable apparatus he can determine the degree of patency of the ostium which would be an important factor in diagnosing disease.

When the diagnosis of frontal sinus disease is in doubt, Hutchinson³⁸ recommends external puncture and aspiration. A trocar is inserted through the floor of the sinus, with the roentgen pictures as a guide. A small incision of the skin is necessary before the trocar is used. The cannula is left in place for the instillation of physiologic solution of sodium chloride, which is then aspirated and examined.

Watkins³⁹ discusses various types of pain in sinuses. Distention of a sinus by pus, gas or swollen membrane causes a sensation of weight or pressure, which is worse in the daytime. If acute exacerbations appear, the pain becomes more intense and is then due to periostitis, osteitis or inflammation of nerves. Pain from distention may radiate over a wide area. Periostitis causes more local tenderness than osteitis. The author believes with Watson-Williams and Pickworth that bacteria may pass from the sphenoid sinus to the pituitary and meninges, giving rise to central pains.

SINUSES IN CHILDREN

Shea's paper⁴⁰ on the treatment of sinusitis in children, which was read at a joint session of the Section on Laryngology and the Section on Pediatrics of the American Medical Association at St. Louis in 1939, evoked considerable controversial discussion, particularly on the question of the nasal pack, the type of shrinking solution and the

36 Seuntjens, H. Biologie quantitative des secretions nasales et sinusiennes, Bull. Soc. Belge d'otol., rhin., laryng., 1939, p. 58.

37 Metz, O. Variations in Respiratory Pressure in Maxillary Sinus, Particularly with Reference to Possibility of Their Application in Diagnosis, Nord. med. (Hospitalltid.) 2: 965 (April 8) 1939.

38 Hutchinson, C. A. External Proof-Puncture of the Frontal Sinus, J. Laryng. & Otol. 54: 259 (May) 1939.

39 Watkins, A. B. K. Neuralgia Due to Sinus Infection, Australian & New Zealand J. Surg. 8: 366 (April) 1939.

40 Shea, J. J. The Rational Treatment of Sinusitis in Children, J. A. M. A. 113: 909 (Sept. 2) 1939.

value of skin tests Dean claimed that the prolonged use of solutions of ephedrine salts was responsible for vasomotor rhinitis in some of the patients whom he had seen. On the other hand, Sweet did not believe that ephedrine was habit forming. On the contrary, he experienced difficulty in having parents continue the use of this drug when it was needed. He stated that the addition of an ephedrine salt, 1 per cent, to an isotonic solution does not change the p_H , because ephedrine is a large organic molecule which does not dissociate into ions. Also he objected to the use of nasal packs in children. Walsh objected to the use of epinephrine on the grounds that Proetz had shown it stops ciliary activity. He suggested the use of the mildest shrinking solutions but failed to state just which solutions he favored. Piness emphasized the role of allergy, having found that over 70 per cent of his children were sensitive to a number of agents. He favors the use of the synthetic ephedrine-like substances as being less sensitive than ephedrine itself. [In defense of Shea it must be pointed out that he has had an extensive experience in treating sinus disease in children, and therefore the multiplicity of therapeutic agents suggested is the result of a sincere effort to afford relief of a state which in many instances is complex and distressing. Naturally, there can be no set rule that is applicable to all cases. Therefore much depends on the physician's ability to appraise accurately the individual pathologic state, the environment, the background and the social status of the patient and apply his therapeutics accordingly. Therapeutic nihilism is just as bad as overtreatment. A happy medium consistent with due regard for natural reparative forces is the ideal all should strive for. S S]

Kerley's paper ⁴¹ is also very comprehensive. He lists the following symptoms which should lead the pediatrician to investigate the sinuses: (1) repeated colds in otherwise healthy children, (2) continuous nasal discharge, (3) severe cough in the absence of pulmonary findings, (4) recurring attacks of otitis, (5) habitual "growing pains", (6) unexplained daily rise in temperature, (7) chronic nephritis and (8) habitual anorexia. He divides the cases into three groups, the frankly allergic, the nonallergic mucoid and the frankly purulent. These are described in detail. For the allergic group he suggests a vaccine containing all the positive allergens, first testing with the 1:10,000 dilution and then giving bi-weekly injections up to 4 minims (0.24 cc), then using the 1:5,000 solution and finally the 1:500 dilution. In most cases he gives sixteen to eighteen injections. At the same time the child is kept in a room from which all possible air-borne allergens have been eliminated. He claims some success in dehydrating turgid

⁴¹ Kerley, D. G. Sinusitis in Children from a Pediatric Standpoint, *Arch Pediat* 55:732 (Dec) 1938.

turbينات by packs of 2 per cent ichthammol N F in 10 to 20 per cent glycerin for ten to fifteen minutes every five days

An analysis of the progress of 100 children by Mitchell⁴² over a period of five years leads him to the conclusion that the removal of tonsils and adenoids in early childhood seems to predispose to sinus infection. He believes that the "sinuses must play an intimate part in immunization from infections of the upper part of the respiratory tract," although the responses to his questionnaire on this subject indicated that only 4 of 15 laryngologists who were addressed agreed with him. He believes with most observers that allergic factors must be sought for and eliminated and he relies on family history, skin tests, eosinophil count and local findings for his diagnosis. He believes that chronic sinusitis in children offers a better prognosis than that in adults. After eliminating the allergic elements and giving adequate local treatment plus the administration of iodides, calcium lactate, thyroid or parathyroid, if the disease fails to yield he advises surgical treatment. He and Shea did 77 antrostomies in 100 cases, removed tonsils or remnants in 36, gave sulfanilamide in 18 and autogenous vaccines in 20. Illustrative cases are cited. He concludes that "the time to prevent infantile sinuses and accompanying sinusitis is during the period of growth and development, that is, during childhood and early adolescence."

Birdsall,⁴³ in an excellent analysis of a large series of cases, finds that roentgen pictures were more than satisfactory since in 35 of 37 cases thus examined they gave positive evidence of sinus disease which was substantiated clinically. In a series of 59 cases treatment yielded 52 cures—34 after a course of displacement therapy, 13 after displacement and lavage and 5 after antrostomy. In 2 cases a Caldwell-Luc operation was required. There is no danger to the tooth buds in the latter operation if the opening is made just below the infraorbital foramen.

In taking roentgen pictures of the sinuses in children Rathbone⁴⁴ advises a fast exposure to prevent blurring. He advises a "large focal spot (2 mm) on a rotating anode shock proof tube, detail intensifying screens, a 7 cm cone and no Potter-Bucky diaphragm." The exposure time for the posterior-anterior projection is one-fifth second and for the lateral one-fifth second, using 350 milliamperes and about 62 kilovolts. The lateral view is important because it includes the pharynx. The author advises removal of large adenoids but favors preliminary roentgen treatment in many cases because it has a beneficial influence

42 Mitchell, E. C. The Treatment of Sinusitis in Children, *J. A. M. A.* **112** 207 (Jan 21) 1939

43 Birdsall, S. E. The Symptoms, Signs and Treatment of Nasal Sinusitis in Children, *J. Laryng & Otol.* **54** 549 (Sept) 1939

44 Rathbone, R. R. Roentgen Diagnosis and Treatment of Chronic Sinusitis in Children, *M. Rec.* **149** 408 (June 21) 1939

on the sinuses as well. Regression of the adenoids took place as a result of this treatment in 25 to 30 per cent of his cases. The dosage recommended is 75 roentgens (r) daily to children under 1 year and 100 r for those between 1 and 5 years of age. Treatments are given three times weekly for two weeks, with exposure of only one area at each treatment.

MacNeil⁴⁵ believes that many chest conditions begin very early in life among children living in poor hygienic surroundings, often following acute exanthems. The sinuses are often too small and underdeveloped to be much of a factor in children under the age of 4. Beyond this period the association of sinusitis and chest disease is more frequent, yet, considering the large number of cases of sinusitis observed, it is remarkable that infections of the chest are considerably less frequent. Nevertheless the author realizes the importance of sinusitis as an etiologic factor in the persistence of thoracic symptoms and advises close study of cases in which these occur.

Miller⁴⁶ is of the opinion that the prognosis of chronic sinusitis is much better for children than for adults if proper treatment is given. Therapy must be persisted in over a long period of time. The recurrence of adenoids is almost a sure indication of sinusitis.

During 1937-1938 at the St. Ladislaw Hospital in Budapest Krepuska⁴⁷ found 61 cases of sinusitis in a series of 7,797 cases of scarlet fever, in 28 of which orbital complications developed. The etiologic factors assigned for the high incidence of this complication are (1) mucosa very rich in blood vessels and lymphatics, (2) large turbinates blocking the sinus ostiums, (3) incompletely ossified bones and (4) incomplete closure of bony sutures.

Torrini⁴⁸ has seen orbital cellulitis in 5 children from 1 to 6 years of age, all of whom were cured without resort to surgery. The classic symptoms observed were a stormy onset during an attack of grip or a cold, pain in the eye, fever and rapid pulse, red tense swelling at the internal angle of the orbit extending to the lids and frequently displacement of the bulb. The absence of chemosis, conjunctival edema and pupillary changes should rule out orbital phlegmon or thrombosis of the cavernous sinus. The treatment included the application of hot wet compresses, frequent nasal shrinkage and suction, and vapor inhalations. If resolution fails to ensue within two or three days, one

45 MacNeil, F. A. Infection in the Nasal Sinuses in Children and Its Relation to Chest Infection, *Manitoba M. Rev.* **19** 201 (Oct.) 1939.

46 Miller, A. B. Sinusitis in Children, *Pennsylvania M. J.* **42** 399 (Jan.) 1939.

47 Krepuska, S. Nasale und orbitale Komplikationen bei Scharlach, *Ztschr. f. Hals-, Nasen- u. Ohrenh.* **46** 175 1939.

48 Torrini, U. L. Sulle celluliti orbitarie nell'infanzia, *Riv. oto-neuro-oftal.* **16** 129 (March-April) 1939.

must be on the alert for signs of suppuration, which would necessitate surgical intervention

Nikhinson⁴⁹ reports 2 cases of orbital abscess in childhood due to ethmoid disease in which the diagnosis was obscured by certain intranasal factors. In 1 case, that of a child of 7, there was a history of trauma followed by abscess of the septum, "empyema of the cribriform plate" and orbital abscess. Recovery followed intranasal incision. The author believes that the infection was primary in the ethmoid cells nearest the cribriform plate and that the other conditions were secondary. In the second case a girl of 15 had an infection of a conchal cell with secondary orbital abscess. The latter ran a protracted course without rise of temperature (cold abscess?).

Wachsberger⁵⁰ believes that susceptibility to sinus disease in children is due to a number of factors, such as the high incidence of the exanthems, the large size of the sinus ostiums and the frequent mouth breathing and impaired ventilation. Recurring infections tend to produce fibrosis, which offers a barrier to further progress. In children the infection hits virgin territory, absorption is more rapid, and therefore the constitutional symptoms are more marked than in older persons.

Blackwell⁵¹ is impressed with the necessity of having the full cooperation of the parents in the treatment of sinus disease in the child, since the diet, hygienic regimen and medication all require constant and careful supervision.

Lanier⁵² presents a number of statistics from the literature bearing on the incidence of sinus disease in children and the percentage of complications. Discussing therapy, he recommends the use of chronic acid crystals for local cauterizations, also, suction, neo-silvol, neo-effemist, iodides and proper hygiene are among the agents for which he finds proper indications. The author believes that roentgen findings may at times be deceptive and must be taken into consideration with all of the clinical findings.

Osteomyelitis of the superior maxilla, a rather uncommon condition, is the subject of several instructive contributions. Asheron's⁵³ article is particularly analytic and thorough and might well serve as a reference work on this subject. He claims that this disease is a staphylococcic

49 Nikhinson, A. G. Orbital Complications of Sinusitis in Children, *Vestnik oftal* **13** 530, 1938.

50 Wachsberger, A. The Significance of Nasal Accessory Sinus Disease in Children, *M. Clin. North America* **23** 681 (May) 1939.

51 Blackwell, K. S. Some Practical Considerations of the Sinuses, *Virginia M. Monthly* **66** 468 (Aug.) 1939.

52 Lanier, L. H. Paranasal Sinus Disease in Children, *Tri-State M. J.* **2** 2222 (Feb.) 1939.

53 Asheron, N. Acute Osteomyelitis of the Superior Maxilla in Young Infants, *J. Laryng. & Otol* **54** 691 (Dec.) 1939.

infection originating in the socket of an unerupted first deciduous molar and the adjacent area of the anterior surface of the superior maxilla. It occurs most often in the early weeks of infancy and up to the first few months of life. The source of the infection is not always clear. It has been attributed to contact with an infected nipple or to trauma at birth with resulting abrasions or extravasation of blood. The antrum becomes involved secondarily, whence the process spreads to the orbit, alveolar process and palate. Abscess formation is observed early, with rupture into the cheek, the gingival recess and the cheek near the internal canthus. The onset is fulminating with septic symptoms. The process must be differentiated from orbital abscess with origin in a sinus, especially the ethmoid sinus. The location of the swelling and the preponderance of orbital symptoms as against symptoms pointing to the cheek, alveolus or palate should make the differential diagnosis easy. Occasionally spontaneous rupture and discharge will be accompanied by amelioration of the symptoms, which will then become protracted, with eventual sequestration. The author reports 4 cases. Only 1 of the patients survived. He recommends prompt external incision below the lower lid with counterdrainage through the orbit into the middle meatus. Also, the palate, gingival recess and antrum may have to be opened. Later one must be on the lookout for sequestrums, which must be removed. Supportive treatment, transfusions, irrigations, frequent dressings and sulfanilamide all have a place in the treatment.

Lacy and Engel⁵⁴ also go into the details of the anatomic pathologic aspects of this grave disorder and list some 70 cases reported in the literature. They believe that drainage is best effected through the gingival recess or intranasally through an antrostomy. One case of their own is reported, being that of a 2 week old infant who when 2 days old had an abscess behind one ear and on the seventh day an abscess of the left buccogingival fold, followed a few days later by swelling of the face and a spontaneous fistula near the internal canthus. Through an antrostomy opening a probe could be passed into the two other external fistulas. The child recovered.

Oreggia⁵⁵ points out the difference between acute osteomyelitis of the superior maxilla and simple acute maxillary sinusitis, emphasizing the necessity for making the diagnosis in view of the gravity of the former condition. He reports the occurrence of acute osteomyelitis of the superior maxilla in 3 children less than 40 days old, due, in all of them, to staphylococcal infection. Two of the children recovered following prompt surgical intervention. The disease in the third child ran

⁵⁴ Lacy, N. E., and Engel, L. P. Acute Osteomyelitis of the Superior Maxilla in Children, *Arch Otolaryng* **29** 417 (March) 1939.

⁵⁵ Oreggia, J. C. Las sinusitis maxilares del niño pequeño, *Arch de pediat d Uruguay* **10** 197 (April) 1939.

a very rapid and malignant course, ending fatally despite active therapy. The type of acute sinusitis which might be confused with osteomyelitis is described in the case history of a child of 16 months suffering from what he calls "exudative diathesis." The symptoms were prolonged febrile periods, profuse secretions more or less mucopurulent and mostly postnasal, spasmophilia, pale mucosa and swollen turbinates. Removal of adenoids often fails to improve the condition, which the author feels is due to a lymphatic diathesis. His recommendations for therapy include active shrinkage with cocaine and ephedrine, short wave therapy and the use of an antiviral. He does not believe that allergy plays much of a role in sinusitis of this type, especially in the younger children.

Kato's⁵⁶ case concerned an infant of 3 months. The disease ran more of a subacute course. There was fever of undetermined origin for two months before swelling appeared in the cheek near the internal canthus, followed by spontaneous rupture and fistula formation. Despite free nasal discharge, the condition was first diagnosed as an infection of a tear sac. Finally, when swelling appeared in the hard palate and was incised and drained without improvement, the patient was brought to the clinic, where the correct diagnosis was made. Ten sequestrums were removed at several sittings, and the patient eventually recovered.

Acuña and Sas⁵⁷ report the case of an infant of 2½ months with no history of previous trouble who suddenly became ill, with high temperature, restlessness and swelling of the left cheek. Within thirty-six hours the edema had increased to involve the whole side of the face, with redness, and there was a profuse purulent discharge from the nose and nasopharynx. *Streptococcus* was present in smear and culture. Treatment consisted chiefly of applications of local heat and nasal irrigations. During the next twenty-four hours the secretion diminished, but new symptoms appeared, viz., edema of the hand and forearm and swelling and ecchymosis of the legs. A transfusion was given. Septic pneumonia developed and death ensued in seventy-two hours. Autopsy disclosed purulent maxillary sinusitis and osteomyelitis, the bone was dark and necrotic. The authors believe that the genesis of this disease may have been in an exacerbation of latent maxillary sinusitis or else that the disease was primary in a dental follicle with secondary spread to the bone and sinus and subsequent general sepsis.

Abt⁵⁸ reports, among his series of cases of allergy, 8 cases of sinusitis in children between the ages of 2½ and 5. These patients were relieved

56 Kato, K. Ein Fall von Sinusitis maxillaris neonatorum, *Oto-rhino-laryng* **12** 562 (July) 1939.

57 Acuña, M., and Sas, B. E. Etmoidosinusitis. Osteomielitis del maxilar superior y septicemia en un lactante, *Arch. argent. de pediat.* **9** 622 (Dec.) 1938.

58 Abt, A. F. Note on Oral Administration of Potassium Chloride in the Treatment of Hay Fever, Nasal Allergy, Asthma and Sinusitis, *Am. J. M. Sc.* **198** 229 (Aug.) 1939.

by the administration of well diluted potassium chloride. Mild diuresis followed the use of this drug. The diagnoses given in some of the cases were "x-ray showed definite cloudiness over the maxillary sinus," "maxillary sinus tenderness," "chronic sinusitis," "chronic sinusitis with nasal polypi," "subacute sinusitis aggravated by use of argyrol," "chronic sinusitis for over one month" and "tenderness over the maxillary sinus and catarrhal congestion" [Harsh and Donovan,⁵⁹ reporting recently, failed to duplicate Abt's results in a series of 40 cases S S]

SINUSES IN RELATION TO DISEASES OF OTHER ORGANS

Ridpath,⁶⁰ who has had long experience in sinus conditions, finds that latent or occult sinusitis is frequently the cause of a wide variety of diseases in regions more or less remote. Heredity as a predisposing factor and the occurrence of numerous infections of the upper respiratory tract early in life are frequently elicited in the history if this is carefully gone into and will often point to the cause of an unexplained infection. Too much emphasis cannot be placed on a thorough analysis of the patient's history. In addition to the well known pulmonary manifestations of sinus disease, the author refers to gastrointestinal disturbances, arthritis, pericarditis and endocarditis as diseases often traceable to chronic antrum infection.

Lathrope, Peer and Paddock,⁶¹ following the same line of thought, state that because of the absence of local symptoms and negative results from irrigation of the antrums many patients come to the internist for relief. Flat roentgen pictures may fail to show tissue changes within the sinus. In latent sinusitis there are few local symptoms, yet the hyperplastic mucous membrane can readily be demonstrated by the use of contrast mediums. Even though the irrigation fluid fails to reveal bacteria, they still may be present in the deeper layers of the thickened membrane, their toxic products being continually absorbed, causing constitutional symptoms. The condition is very similar to certain infections of the gallbladder. Four typical cases are cited, with complete relief following repeated irrigations, instillation of iodized poppyseed oil and the use of argyrol packs. In a series of 100 cases of chronic disease of the antrum, suppurative in 50 and hyperplastic in 49, the chief subjective symptoms elicited were lassitude (82), repeated colds (63), rheumatic pains (50), cough (36), indigestion (33), loss of weight (23), asthma (14) and hay fever (8).

59 Harsh, G. F., and Donovan, P. B. Potassium Chloride in Allergic Disorders, *J. A. M. A.* **114** 1849 (May 11) 1940.

60 Ridpath, R. F. The Role of the Sinuses in General Medicine, *M. Times*, New York **67** 154 (April) 1939.

61 Lathrope, G. H., Peer, L. A. and Paddock, R. The Importance to the Internist of Latent Paranasal Sinusitis. *Ann. Int. Med.* **12** 1576 (April) 1939.

Pulmonary Disease—Smith⁶² and Comee⁶³ both review the literature on pulmonary complications of chronic sinus disease and emphasize the importance of thorough investigation of the sinuses in all chronic cases. Smith states that since the mucosa throughout the respiratory tract is similar the reaction is the same in all locations. The problem therefore overlaps several specialties, and there is always the danger that too much emphasis from one point of view may be detrimental to the patient's best interests. Repeated examinations and consultations between rhinologist, internist and roentgenologist are often necessary before deciding on a course of therapy.

Nakamura⁶⁴ reports 15 cases of chronic bronchitis in association with sinus disease. Three of the patients had asthmatic symptoms, and nearly all had bilateral involvement. The type of sinusitis found was suppurative in 12 and nonsuppurative in 3. Most of the patients were undernourished and neurotic.

Chipman and Collins⁶⁵ report on the material seen at the St. Johns Clinic for tuberculosis from 1931 to 1938, during which period 4,005 new patients were examined, 2,670 being found nontuberculous. Five hundred and ninety-seven patients were examined for sinus disease, 59 per cent of whom revealed definite evidence of infection. There were 58 patients with bronchiectasis, 28 of whom had neither sinusitis nor pneumonitis, 4 had pneumonitis, 5 had pneumonitis and sinusitis, and 21 had sinusitis alone. Thirty-six patients with pneumonitis and 68 with sinusitis were found to have one or the other of the three conditions frequently in association, which impressed the authors with the necessity for early diagnosis and removal of septic foci from the sinuses. "Until we know what proportion of our population in all age groups have sinusitis, it is impossible to state whether patients with T. B. have an unusually high percentage of sinusitis. We see no reason to suspect that this is so. Of our 116 proved cases of sinusitis, pneumonitis or bronchiectasis only five children had definitely active T. B. Of the adult group, 24 patients had T. B."

Mounier-Kuhn⁶⁶ claims that the association of sinusitis and bronchial involvements can be explained in different ways. The bronchial disease may be purely coincidental, or due to a descending infection or to aspiration, or to transmission by way of the lymphatics, or it may be

62 Smith, A. T. The Relation of Chest Conditions to Sinus Disease. The Otolaryngologist's Point of View, *Laryngoscope* **49** 1134 (Nov.) 1939.

63 Comee, W. C. Chronic Suppurative Sinusitis. Its Relation to Pulmonary Disease, *Wisconsin M. J.* **38** 549 (July) 1939.

64 Nakamura, S. Relation of Chronic Bronchitis and Paranasal Sinusitis, *Ztschr. f. Oto-Rhino-Laryng.* **45** 5 (May) 1939.

65 Chipman, L. DeV., and Collins, R. J. Bronchiectasis and Tuberculosis in Relation to Nasal Sinusitis, *Canad. M. A. J.* **40** 557 (June) 1939.

66 Mounier-Kuhn, P. Sur la coincidence d'une affection nasale et d'une suppuration broncho-pulmonaire chroniques, *Lyon med.* **163** 413 (April 9) 1939.

a congenital condition as proposed by Kartagener⁶⁷, or the sinus condition may be secondary to the bronchopulmonary infection and caused by expectoration of secretions [The last-mentioned theory is attributed to American authors, who are not named One wonders where he got the idea! S S] The author cites 7 cases, 4 of bronchiectasis and 3 of purulent bronchitis Nasal examination revealed polypoid sinusitis in 5, chronic maxillary sinusitis in 1, and in the seventh case the bronchial condition followed operation on the tonsils and adenoids In common with other authors, previously quoted, he finds that the nasal symptoms were minimal in most of his cases, which again emphasizes the importance of careful examination of the sinuses in all patients with chronic bronchitis and other nontuberculous pulmonary diseases Discussing the therapy of these conditions, the author suggests the use of sulfur inhalations as described by Pouillet

Tsigelnik⁶⁸ mentions the two principal routes of infection from the sinuses to the chest, namely, by way of the respiratory tract, through aspiration, and by way of the lymphatics He believes the processes may develop simultaneously during an attack of grip or measles In some cases there is a hereditary predisposition, since he has found anomalies in other locations in some of his patients In a series of 130 cases of bronchiectasis recorded by the author there were 35 in which this condition was associated with definite sinus disease, in 23 of which the sinus involved was the antrum He depends on roentgen studies with contrast mediums both in the sinuses and in the bronchial tree for his diagnosis

Bettington⁶⁹ reports a case in which long-standing bronchiectasis in a woman of 44 failed to improve after several bronchoscopic aspirations and instillations of iodized poppyseed oil A later examination revealed cloudy antriums Radical exposure showed both sinuses lined with a hyperplastic polypoid mucous membrane Operation was followed by general improvement, with lessening of the cough A cure was not expected because of the chronicity of the process, but the author wonders whether earlier discovery and eradication of the foci in the sinuses might not have achieved such a result in view of the marked improvement obtained even at a late date

Nuhsman⁷⁰ presents a chronologic list of references on the subject of sinusitis in relation to asthma and cites 2 cases in a series of 12 from

67 Kartagener, M, and Ulrich, K Bronchiectasien und Veränderungen der Nasennebenhöhlen, *Ztschr z Klin d Tuberk* **86** 349, 1935

68 Tsigelnik, A Y Chronic Sinusitis and Bronchiectatic Disease, *Sovet vrach, zhur* **42** 649 (Nov 15) 1938

69 Bettington, R H A Case of Bronchiectasis of Long Standing and Unsuspected Maxillary Antritis, *M J Australia* **26** 545 (Oct 7) 1939

70 Nuhsman, T Zur Behandlung des rhinogenen Asthmas, *Arch f Ohren-, Nasen- u Kehlkopfh* **146** 209, 1939

his own experience. In the first instance a woman of 39 had had asthma for fifteen years. It was often severe enough to put her to bed. Several minor nasal operations had given only temporary relief. Finally a radical exenteration of the polypoid tissue of the ethmoid cells and antrums was performed, with complete relief, the patient being free from symptoms when seen one year later. In the second, a man of 54 had asthmatic symptoms dating back nine years to an attack of grip. Numerous minor operations on the nose were fruitless, and it was only after complete exenteration of several diseased sinuses that the patient obtained relief. The author claims equally good results in 9 other cases. Recurrences could always be traced to incomplete removal of diseased tissue at operation. The author is convinced that allergy, when present, is incited by the existing infection, and he feels that the only way to cure these patients is by thorough and complete eradication of the mucosa of the diseased sinus.

Russell⁷¹ expresses the same conviction in another way. He believes that in many cases the disease begins in childhood, due to an unresolved sinus infection, as a result of which the mucosa is left in what he calls a state of "touchiness." Therefore, what we call allergy is in some cases merely a hypersensitive state of a mucosa previously damaged by infection. He amplifies this by saying "one might restate the case in another way by saying that certain types of inflammation are capable of injuring the protoplasm in a specific way so that certain unsatisfied haptophore groups are left sticking out, as it were, eager to hook on to the benzene-ring portion of appropriate antigens." In a series of 50 cases Russell finds a close association between the condition of the sinuses and asthma, although from this limited experience he cannot state positively that the former is fundamental. The essential lesion found in the sinuses is edema, often reaching polypoid development. Pus is infrequent, and the usual symptoms of sinusitis are absent. He finds the use of contrast mediums very helpful in determining the state of the sinus mucosa and shows a number of roentgen pictures illustrating typical cases.

Harrington⁷² is averse to surgical intervention and prefers conservative treatment of the nose in cases of asthma. He suggests a number of procedures, including displacement therapy and the use of the Dowling pack. He is very enthusiastic about the latter and goes into much detail as to its application. Also, much space is given to a description of Gautier's diastolization, which is a form of intranasal massage by means of inflated rubber bougies shaped to fit the nasal fossae. The

⁷¹ Russell, H. G. B. Observations upon the Nasal Aspect of Asthma, *St Barth Hosp Rep* **72** 23, 1939.

⁷² Harrington, F. T. Investigation and Conservative Treatment of the Nasal Factor in Asthma, *Indian M Gaz* **73** 725 (Dec.) 1938.

inflated bougie is allowed to remain in the nose for a few minutes to compress the mucosa. The air is then withdrawn and the tube removed. Then it is again passed in and out of the nose under various degrees of inflation, thirty to forty times, thus massaging the tissues. A flow of mucus is brought about, which is finally expelled by the patient. A course of treatment consists of twenty applications given at the rate of three a week, the size of the bougie being increased as the shrinking tissues permit. Another therapeutic measure recommended is the inhalation of vapor impregnated with papaverine and ephedrine.

Agar and Cazort⁷³ having observed a number of allergic patients with nasal disease are inclined to be conservative in their treatment of the sinuses. They claim never to have found it necessary to do a radical operation, having had good results by way of minor procedures, such as submucous resection, cauterization, removal of polypi and antrostomy. They stress the importance of cytologic examination of the nasal secretions in the diagnosis. [The opposing views of the aforementioned authors on the subject of asthma and sinusitis are due to the fact that each one's experience has been predominantly with one type of asthma to the apparent exclusion of the other type. Between the extremes of pure allergy and total infection one may find combinations of the two in various degrees. Hence the variety of deductions depend on the predominating types with which the authors have had the most experience. S S.]

Arthritis—Hamblen⁷⁴ speaks from an experience gained at a rheumatism clinic, where 18 per cent of the patients referred to him had sinus disease. A cure or a definite improvement of the rheumatic process was obtained in 70 per cent of the patients treated. Included under the diagnosis of rheumatism were all types of arthritic inflammation except, in a few cases, osteoarthritis. The principal organisms found in drainage of the sinuses were *Streptococcus haemolyticus*, *Streptococcus viridans* and *Staphylococcus*. When there was a history of a severe cold or grip antedating the onset of the arthritis, one could usually find persisting sinusitis as the etiologic factor. Frequently there was an association of chronic sinusitis with sore throat or recurring attacks of tonsillitis. Significant signs to be observed are redness and swelling of the lateral pharyngeal bands, a glazed posterior pharyngeal wall, small tender postcervical glands and stiffness of the neck muscles. Conservative treatment is advised for infirm and debilitated patients. Otherwise surgical operation is indicated if the roentgen studies with contrast mediums reveal osteitis or marked changes in the mucosa of the sinus.

⁷³ Agar, I. S., and Cazort, A. Pathologic Nasal Conditions Affecting Clinical Allergy, *South M J* **32** 1063 (Oct.) 1939.

⁷⁴ Hamblen, T. C. Nasal Catarrh and Nasal Sinusitis in Their Relation to Chronic Rheumatism, *J. Roy. Inst. Pub. Health & Hyg* **2** 11 (Jan.) 1939.

Based on a study of 100 consecutive cases of infectious arthritis, in 20 of which there was positive evidence of sinus disease, Williams and Slocumb⁷⁵ make the statement that "it would seem to be an error to assume that the sinuses can be ignored as possible foci of infection" In 19 of the 20 cases mentioned, positive roentgen pictures were obtained Of 12 patients who were operated on, 6 obtained complete relief, but since 4 of these had their tonsils removed at the same time, it is difficult to say which was the real focus of infection In the authors' experience it was apparent that if relief failed to follow the operation on the sinus within two weeks, no further improvement could be looked for Most of the sinuses operated on were frankly purulent, there being only 3 instances of the so-called silent type of sinusitis

Neurologic Disorders—Porta⁷⁶ contributes a long dissertation on the relationship between chronic ethmoiditis and certain neurologic and psychologic disturbances, citing a number of references from the literature having to do with specific cases that were apparently proved as well as with the topic in general The routes by which infection may be transmitted are described as follows (1) through perisinus reaction resulting in modification of the thickness of the bony walls with encroachment on adjacent tissues, (2) local meningeal reaction by extension of a periosteal inflammation, (3) diploetic reaction with secondary involvement of perforating communicating veins, (4) reaction in the skull base with condensing osteitis, diffuse or circumscribed, resulting in compression of basilar structures, (5) generalized reaction of the organism with specific alteration of hypophyseal function Experiments on rabbits show that infections introduced into the vault of the pharynx and the sphenoid sinus produce inflammatory reaction in the pituitary and other nerve structures of the base Much space in the article is given over to the details of the procedures the author recommends for the determination of the metabolic and endocrine functions, in addition to the usual neuropsychic examination, all of which are well known to most neurologists and internists Specifically, the author cites several cases among the 9 which he studied and in which definite disturbances of a trophic and metabolic nature were traced to chronic infection of the posterior sinuses

Osteomyelitis—Laskiewicz⁷⁷ presents a number of case histories with photographs of the patients and histologic sections of bone tissue He is convinced from his experience that the chief route of infection is by way of the diploetic veins, especially the Breschet plexus, which

75 Williams, H L, and Slocumb, C H Nasal Accessory Sinuses as Foci of Infection in Arthritis, *Arch Otolaryng* **29** 829 (May) 1939

76 Porta, C F Sul comportamento del sistema neurovegetativo diencephalico ed extradiencephalico nelle sinusiti, *Arch ital di otol* **51** 163 (April) 1939

77 Laskiewicz, A Les osteomyelites des os plats du crâne d'origine nasale et otique, *Rev de laryng* **60** 185 (March) 1939

cross interosseous sutures, although he also recognizes that in some cases the spread is along the periosteal and endosteal plane. The former route accounts for involvement apparently remote from the original focus, while the latter explains the localized large periosteal and extradural accumulations of pus. Contributing factors are local conditions favoring retention of pus within the sinus, such as marked septal deviation, occlusion by a middle turbinate, constriction or tortuousness of the nasofrontal duct, inadequate or ill timed surgical operation or trauma in the presence of infection. The author finds two principal types of bone lesion. In one there is considerable edema of the medullary structure with marked round cell infiltration. The blood vessels are occluded by recently formed thrombi. This type is usually accompanied by extensive suppuration. The other form is characterized by more extensive destruction of bone, with numerous foci of resorption, areas filled with osteoclasts, numerous bacteria, large amounts of detritus and at the same time areas showing evidence of new bone formation. The necrotic areas are naturally in the external or internal plates and lead to sequestration. The medulla being more vascular generally offers more resistance to the spread of the process, which in this type tends to become chronic. The author prefers the Jacques modification of Jensen's technic, leaving a large opening at the internal angle for free drainage and inspection. He also uses roentgen rays, short waves and Delbet's vaccine or an autovaccine. One of the roentgen pictures presented by the author shows very clearly the dilated Breschet veins coursing through the diploe.

Skullern⁷⁸ cites 6 cases and discusses the pathologic aspects and the routes by which the infection spreads. He prefers the "trans-eye-brow" incision and removal of the anterior wall of the frontal sinus to permit adequate inspection and space for dealing with the disease. If the dura is exposed, he covers it "with strips of sheet rubber which in turn is covered by a single layer of gauze which is kept saturated every second hour with lysated organismal fluid. The periosteal skin flap is closed over the dressings with drainage through the temporal incision." At a secondary operation, when the wound has ceased to suppurate, thin spicules of bone derived from the edges of healthy bone are spread over the dura, which speeds up the regeneration of the bony plate. In all cases the nasofrontal duct is enlarged and drainage into the nose facilitated.

The 3 cases described by Arauz, Mercandino and Belou⁷⁹ were all different. In the first case the osteomyelitis followed acute frontal sinusitis, the process attacking the outer layer of bone near the external

78 Skullern, S. R. Osteomyelitic Invasion of the Frontal Bone Following Frontal Sinus Disease, *Ann Otol, Rhin & Laryng* **48** 392 (June) 1939.

79 Arauz, S. L. Mercandino, C. P., and Belou, A. P. Consideraciones a proposito de tres casos de osteomyelitis del frontal, *Rev. Asoc. med. argent* **53** 602 (Jul. 15) 1939.

orbital angle In the second case the process was metastatic from an osteomyelitic focus elsewhere plus local trauma, and in the third case the osteomyelitis occurred during chronic frontal sinusitis following previous incision of a subperiosteal abscess All the lesions were treated by wide excision with open drainage Two patients required subsequent plastic procedures

Hirst⁸⁰ reports the case of a patient who was operated on six times, finally succumbing to the disease An acute infection involved the frontal and maxillary sinuses, with local edema and tenderness, and was treated at first by intranasal antrostomy and infraction of the middle turbinate A few days later the frontal sinus was opened through the anterior wall, which the author concedes may have been an error, since it would have been safer to trephine through the compact bone of the sinus floor rather than the cancellous anterior plate [The best authorities agree that in severe acute frontal sinusitis it is perfectly safe to trephine through the floor of the sinus near the inner angle, for drainage only, care being taken not to crush the bone or attempt to curet either bone or swollen mucosa S S] Subsequent operations were done in an attempt to halt the process, which eventually involved the endocranium and resulted fatally

Ballenger⁸¹ reports 5 cases of osteomyelitis involving the sphenoid and states that the diagnosis before intracranial complications have set in is very difficult One finds the usual vague symptoms of sphenoiditis, such as postnasal discharge deep-seated headache, retro-orbital pain, photophobia, lacrimation, scotomas, etc Roentgen pictures are helpful but not conclusive The sella turcica may show calcification of the bridge or of the ligaments going to the clinoid processes In four of the author's cases there was concurrent otitis media with involvement of the mastoid or petrous bone, which complicated the picture so that it was difficult to trace the exact course of the bone involvement Autopsies showed that extension to the meninges took place by way of the sphenoid bone directly in 2 cases, the cavernous sinus in 1 case and the petrous bone in 2 cases Pneumococci of type III were present in 4 cases and *Streptococcus haemolyticus* in 1

If the disease is unilateral, King⁸² advises a flap with a temporal pedicle An attempt is made to obliterate the sinus, the wound is packed for six days, during which time dilute solution of sodium hypochlorite is used freely After suppuration has ceased, the wound is closed

80 Hirst, O C Osteomyelitis of the Skull Complicating Mastoiditis and Frontal Sinusitis, *Arch Otolaryng* **29** 24 (Jan) 1939

81 Ballenger, H C Osteomyelitis of the Sphenoid Bone Report of Five Cases with the Autopsy Findings, *Ann Otol, Rhin & Laryng* **48** 95 (March) 1939

82 King, J E J Osteomyelitis of the Skull, *Laryngoscope* **49** 405 (May) 1939

Takamura⁸³ reports a case of osteomyelitis of the upper jaw following intranasal antrostomy. The symptoms were a foul bloody discharge, chills, a high temperature and external swelling appearing within twelve hours after operation. A fistula appeared near the internal canthus, discharging pus. Later a sequestrum was found in the nose, the bony septum became necrotic, and the process spread to the palate, resulting in necrosis with a large perforation. Later the entire superior maxilla became involved, resulting in death from sepsis fifty days after the operation. [Although the details of the original surgical procedure were not given, it is well to point out that the use of a rasp for the antrostomy, particularly when the involvement is still subacute, has been known to be the means of infecting the bony nasointral wall, setting up this extremely dangerous and generally fatal disease. S S.]

Ision Ponte⁸⁴ reports a rather rare occurrence—osteomyelitis of the superior maxilla as a sequel of a Caldwell-Luc operation. The symptoms appeared one week after the operation, with pain and foul discharge. The operative site was inspected and an area of dead bone encountered. The Wassermann and Kahn tests were found strongly positive. Energetic antisyphilitic treatment effected a prompt cure. As a result of this experience, the author was impressed with the importance of a routine preoperative Wassermann test.

Harrison's⁸⁵ case was one of a cold followed by the usual symptoms of acute osteomyelitis of the frontal bone. A subperiosteal abscess was found, the bone was red but pitted on pressure, and the sinus was full of pus. The external table was removed completely, and ethmoid cells were cleaned out. The patient was operated on again two days later when more bone was removed and more adequate drainage effected. Recovery ensued. [There was no mention of roentgen studies in this case. S S.]

Orbital and Ocular Complications—Escat⁸⁶ presents his sixth contribution on the relationship of the posterior sinuses to optic neuritis and states that he has operated on 49 apparently healthy sinuses with increasingly better results. The operation consists of the removal of

83 Takamura, S. Ein Fall von Osteomyelitis des Oberkiefers im Anschluss an intranasale Operation bei Kieferhöhlenempyem, Oto-rhino-laryng 12 14 (Jan) 1939

84 Ision Ponte, A. Complicações post-operatorias da sinusite maxilar. Osteite sífilica, Rev. med. brasil 4 115 (May) 1939

85 Harrison, H. H. A Case of Osteomyelitis of the Frontal Bone Complicating Left-Sided Frontal Sinusitis. Australian & New Zealand J. Surg. 8 313 (Jan) 1939

86 Escat, E. Action abortive sur l'évolution des névrites optiques de l'éthmoïdo-sphénoïdectomie en cavité nasale saine. Essai d'interprétation physiopathologique, Ann. d'oto-laryng., July 1939, p. 637

the middle turbinate and making as large an opening into the sphenoid as possible. Discussing many theories as to the reason for the favorable reaction on the ocular apparatus, the author advances his own explanation to the effect that the resolution of the neuritis is due to phlogosis in the ethmoid and sphenoid regions resulting from the trauma of the operation. Specifically, it is the trauma to the neural mechanism of the trigemino-sympathetic nerves by way of the sphenopalatine ganglion acting on the optic nerve through their intimate neural connections that brings about resolution.

Kretzschmar and Jacot⁸⁷ present several cases in which the findings were typical of the syndrome of the sphenoid fissure described by Terrien in 1925. The usual symptoms are ptosis, exophthalmos with ophthalmoplegia, fixed dilated nonreacting pupil, anesthesia of the cornea and impairment of vision—in other words, symptoms of pressure on the structures passing through the fissure. The etiologic factor may be trauma, pressure of a neoplasm, syphilis or some undetermined origin. The authors believe that sphenoiditis may also lead to this condition by extension of osteoperiostitis to involve the margin of the fissure. One case was that of a woman of 43 who had been under treatment off and on for ten years. Eventually ophthalmoplegia developed with exophthalmos, paralysis of the third and fifth nerves and retrobulbar neuritis. Roentgen pictures showed the area medial to the orbital fissure to be cloudy and all the margins indistinct. There was a zone of decalcification present. Also at the bottom of the orbit there seemed to be a dark gray zone, 2 cm. in diameter, having its center at the inferior angle of the sphenoid fissure, which might be a tumor. Several operations were performed on the frontal, maxillary and sphenoid regions, disclosing thickened inflamed mucosa. The authors decided then that the shadow was due to osteoperiostitis from the chronic sinusitis. All of the symptoms improved except the ptosis and impaired visual fields. They believe that the incompleteness of the result is to be ascribed to the fact that the condition had become chronic before radical measures were undertaken. The second patient had had symptoms for two years, namely, proptosis, corneal anesthesia, paralysis of the oculomotor nerve and central scotoma. Chronic pansinusitis was present, with frank pus and polypi. Radical surgical operation on the sinuses resulted in complete recovery. In the third patient, with similar symptoms, the sinuses appeared to be normal, but the roentgen films showed cloudiness in the apex of the orbit. Submucous resection and opening of the sphenoid sinus resulted in rapid improvement, the ptosis and the paresis

87 Kretzschmar, S, and Jacot, P. Des symptômes précoces et d'une étiologie souvent méconnue du syndrome de la fente sphénoïdale, *Schweiz. med. Wchnschr.* 69 1103 (Nov. 4) 1939.

of the superior rectus muscle being the last to clear up. In the fourth patient the antrum and ethmoid cells were definitely infected. Operation on this patient also resulted in resolution of the ocular troubles. The authors conclude that when syphilis, trauma and tumor have been excluded, one should not hesitate to open the sinuses even if gross evidence of disease is lacking.

Cone, Moore and Dean⁸⁸ have found laminagraphy, or "body section radiography" as they term it, far superior to the routine roentgenologic technic for showing changes in the sinus interior, especially the posterior group. They describe 5 typical cases of retrobulbar neuritis in which the nasal symptoms were minimal and demonstrate the laminagraphs which revealed the exact location of the occult disease in the sinus responsible for the neuritis, as proved by subsequent operation.

Dvorzhats⁸⁹ finds the incidence of sinusitis in connection with optic neuritis to be 20.9 per cent. The symptom of van der Hoeve was present more frequently than the Birch-Hirschfeld syndrome.

Cullom⁹⁰ is convinced that there is a close association between optic neuritis, toxic amblyopia and sinus disease and presents 6 cases with positive roentgen findings to support his contention. Four were cases of progressive toxic amblyopia with marked visual impairment, 1 was a case of long-standing inflammation of the vitreous, and 1, of optic neuritis associated with unresolved empyema of the sphenoid. Operation disclosed marked pathologic change in the sinuses in every case, and recovery was prompt following the operation.

Nakamura⁹¹ reports a case of retrobulbar neuritis of several months' duration due to chronic suppurative maxillary sinusitis. Bilateral radical operation resulted in prompt recovery. In a case with similar findings the patient refused operation but recovered nevertheless, following a number of irrigations of the antrum.

Zambrini's⁹² patient, a woman of 50, suffered from severe frontal headaches and ocular pains for over a year and then suddenly lost her vision. A large central scotoma was found, and roentgen examination

88 Cone, A. J., Moore, S., and Dean, L. W. Relationship of Paranasal Sinus Disease to Ocular Disorders. New Critical Method of Investigation by Laminagraphs, *Laryngoscope* **49** 374 (May) 1939.

89 Dvorzhats, A. Van der Hoeve, Birch-Hirschfeld in Rhinogenic Inflammation of Optic Nerve, *Vestnik Oftal* **15** 105, 1939.

90 Cullom, M. M. The Effect of Sinus Disease on the Eye, *South M. J.* **32** 743 (July) 1939.

91 Nakamura, K. Rhinogene Sehnerventzündung, *Oto-rhino-laryng* **12** 556 (July) 1939.

92 Zambrini, A. R. Neuritis retrobulbar operada, *Rev. Asoc. méd. argent* **53** 34 (Jan. 15) 1939.

revealed bilateral cloudy sphenoid sinuses. These were opened via the transeptal route, with prompt relief from the pain and return of vision within one month.

Lagrange and Goulesque⁹³ report 3 cases of iritis, in 2 of which the Wassermann reaction was positive. The ocular complication failed to yield to antisyphilitic treatment but cleared up completely after operation on the diseased maxillary sinuses. The authors discuss theories of the pathogenesis in these cases. The hemosporic theory explains metastatic localization but does not give the key to the connection between the two foci. The reflex theory, illustrated by the successful results obtained by injections of cocaine within the orbit and, conduction along the afferent fibers of the trigeminal nerve to the ocular bulb does not explain focal iritis from distant foci. The allergic theory is based on the clinical subordination of the secondary focus and might explain the pathogenesis but does not account for certain elective localizations. The authors believe the answer to the latter objection is the fact that the ciliary body contains an abundance of reticuloendothelial tissue which is capable of fixing the allergic factor in the ocular area. This would confirm the presence of a general pathologic state but opposes the conception of a pathologic reaction as from a specific germ on the idea of a specific morbidity.

Chavanne and Colrat⁹⁴ describe a case in which two weeks after the removal of numerous nasal polyps there was a sudden appearance of blindness in one eye due to a macular hemorrhage, which was seen in the preretinal area. A narrow strand of blood extended to the margin of the disk which appeared normal. The hemorrhage was completely absorbed in six weeks. The patient had no hypertension, albuminuria or other vascular disease. The authors state they could find no record of any similar case in the literature.

A difficult case came under the observation of Emiliani and Bisi⁹⁵. An intranasal operation on the ethmoid cells was undertaken for the relief of chronic suppuration but had to be abandoned because of excessive bleeding, which necessitated packing. A short time later there was a rise in temperature, pain in and about the eye and slight edema. The pack was removed the next day, but the orbital symptoms increased in intensity. Chemosis, proptosis, ophthalmoplegia, steamy cornea and optic neuritis all appeared within a short time. An external

93 Lagrange, H., and Goulesque, J. Iritis et infection focale, allergie système reticulo-endothélial, clasogénnes, *Bull. et mem. Soc. franç. d'opht.* **51** 334, 1938.

94 Chavanne, F., and Colrat, A. Infection naso-sinusienne. Hémorragie maculaire prérétinienne, guérison, *Oto-rhino-laryng. internat.* **23** 225 (May) 1939.

95 Emiliani, C. M., and Bisi, R. Absceso del vertice de la orbita postetmoidectomia, *Rev. oto-neuro-oftal.* **14** 106 (April) 1939.

incision exposing the lamina papyracea failed to reveal any pus. Incision through the periorbita, however, reached an abscess at the apex of the orbit, which was drained with difficulty, resulting in eventual recovery.

Uren⁹⁶ reports 3 cases of orbital complications from disease of the frontal sinus, following swimming in 2 of them. In the first case there were symptoms of early thrombosis of the cavernous sinus, with chemosis, edema and paralysis of the fourth and sixth nerve. Prompt external drainage was followed by recovery. In the second case an orbital abscess ruptured spontaneously into the nose. In the third case the disease was fulminating in onset, the patient becoming comatose and showing flaccid paralysis of the right extremities and of the facial nerve on the right, in addition to local edema and ptosis. The spinal fluid was turbid, and the temperature was 104 F. Improvement followed several spinal taps. Two or three months later osteomyelitis with local necrosis was discovered, but the patient refused operation because he felt too well. The author stresses the value of early symptomatic treatment and the use of sulfanilamide.

A very interesting case of bilateral accommodation paralysis and unilateral scotoma due to sphenoid disease in a man of 20 is reported by Elles⁹⁷. Despite careful opening of the sphenoid and posterior ethmoid cells, the symptoms failed to disappear. Additional roentgen studies by Schuller revealed a pterygoid extension of the sphenoid, which had evidently been previously missed. Oscar Hirsch then operated by the transeptal route and found a complete horizontal partition in the sinus, below which was a large compartment extending into the pterygoid, containing a yellowish fluid. Both sphenoid sinuses were thrown into one cavity, and within an hour the patient could read fine print. The recovery was complete.

Among the cases reported by Srinivasan⁹⁸ was one in which a bluish elevation developed at the inner end of the upper eyelid of a boy of 9. This proved to be a hemorrhage due to scurvy, which improved when the diet was corrected. Another case was that of a boy who had a persistent edema of the right upper eyelid for six months. The child was also asthmatic. A large myxomatous middle turbinate and several polyps were removed, with immediate relief of the ocular symptoms as well as of the asthma.

96 Uren, C. T. Serious Complications of Frontal Sinus Disease, *Ann Otol, Rhin & Laryng* **48** 515 (June) 1939.

97 Elles, N. B. Bilateral Accommodation Paralysis and Unilateral Scotoma in Sphenoidal Sinus Disease, *Am J Ophth* **21** 1365 (Dec) 1938.

98 Srinivasan, E. V. The Relation of Eye to Ear, Nose and Throat, *Antiseptic* **36** 469 (June) 1939.

Sobol⁹⁹ reports 10 cases of sinusitis with orbital complications, due mostly to grip. Two of the patients died.

Intracranial Complications—Yaskin¹⁰⁰ presents an exhaustive review of the material at the Graduate Hospital and the Northern Liberties Hospital, covering a period of twenty years. A total of 443 intracranial neurologic complications of otitis and sinusitis were studied, 91 of which were due to the latter. The discussion includes modes of transmission, symptoms, diagnosis and treatment. Emphasis is placed on the finding of multiple complications in many cases, and the necessity for early and frequent spinal puncture in all cases in which the diagnosis is in doubt is stressed. Five cases of extradural abscess of sinus origin were seen, the condition resulting fatally in all. In 2 the abscess was associated with thrombosis of the longitudinal sinus, in 1, with abscess of the brain, and in 2, with meningitis. Four cases of pachymeningitis interna with subdural abscess of sinus origin were observed. The symptoms are hard to differentiate from those of an extradural abscess. The condition usually results from the latter by direct extension with or without fistula. Three of the 4 patients recovered. Eleven cases of protective meningitis were seen, in 2 of them the meningeal disease was due to sinusitis. All of the patients recovered. This type of meningitis is differentiated from bacterial meningitis by the absence of bacteria and the chemical changes usually associated with the latter.

A total of 196 cases of bacterial meningitis are included in the series, in 31 of which the condition was due to sinusitis. There were 16 cases of brain abscess due to sinus disease, in 14 of which the abscess originated in a frontal sinus, only 3 of the patients survived. Contralateral involvement is explained as being due to thrombophlebitis or to deviation of the intersinus septum. A history of a definite chill or grippy feeling was quite common in these cases in contrast to those of abscess of otitic origin, in which a chill was rare. Also the symptoms of intracranial pressure were quite constant. Three cases of nonsuppurative encephalitis are described in detail. In these cases there were focal symptoms without evidence of pressure, slight fever and leukocytosis. Two cases of thrombophlebitis of the cavernous sinus were found in the series, and 2 cases of thrombophlebitis affecting the longitudinal sinus. The author presents abstracts of the histories of 19 cases, which are illustrative of the various types of complications and are worthy of careful study.

99 Sobol, I. M. Clinical Observations on the Role of Sinuses in Complications of Orbital Inflammation, *Vestnik oftal* **13** 451, 1938.

100 Yaskin, J. C. Neurologic Complications of Infections of the Temporal Bone and Paranasal Sinuses, *Arch Otolaryng* **30** 157 (Aug.), 360 (Sept) 1939.

Statistics from the otolaryngologic clinic of the Sabbatsberg Hospital, in Stockholm, Sweden, since 1912, presented by Sjöberg,¹⁰¹ show that of a total of 41,895 patients admitted, acute frontal sinusitis was present in 1,958 (4.6 per cent). Eight of these had an abscess of the frontal lobe, and only 1 in this group recovered. Chronic frontal sinusitis was present in 3,364 (8.1 per cent) of the patients, 8 of whom had abscess of a frontal lobe. The mortality was 62.5 per cent (5 cases). One case in which the abscess was due to acute frontal sinusitis and in which recovery took place is described in detail.

After describing 3 cases of abscess of a frontal lobe due to frontal sinusitis, Carrascosa¹⁰² draws the following conclusions: 1. Metastatic abscess is thrombophlebitic in origin and apoplectiform in onset. 2. Abscess occurs most often in acute sinus disease or acute exacerbation of chronic sinusitis. 3. One may suspect its presence if unable to explain a sudden exacerbation of the original complaint in the absence of other findings elsewhere. 4. The sudden appearance of somnolence or psychic disorders in the absence of osteomyelitis or meningitis is extremely suggestive of abscess of the brain. 5. Metastatic cerebral abscess is more common than generally supposed. Case 1 was an instance of acute frontal sinusitis with bilateral frontal lobe abscess. Case 2 was an instance of an exacerbation of chronic frontal sinusitis with an abscess in the temporal region. Case 3 was a case of frontal sinusitis complicated by mucocele and abscess of the frontoparietal region of the brain. All the case histories are quite typical, showing that when the abscess encroached on the temporal region the focal symptoms were definite whereas when it was restricted to the frontal area the symptoms were chiefly those of encephalitis.

A case in which the diagnosis was obscured by the history of a mastoid operation several years ago is described by Kepes.¹⁰³ A 14 year old boy with acute frontoethmoiditis began to have meningeal symptoms and signs of a left temporal abscess. Operation on the sinuses revealed an acute purulent infection, but exposure of the dura failed to show any abnormality. The author therefore felt that the cerebral symptoms must have originated from a focus in the old mastoid area of infection, and therefore the mastoid wound was reopened and the dura exposed. It was found to be bulging and when incised revealed a cortical abscess. The patient, however, succumbed, and the

101 Sjöberg, A. A. A Contribution to the Prognosis and Treatment of the Rhinogenous and Otogenous Brain Abscesses, *Acta oto-laryng* **27** 638, 1939.

102 Carrascosa, A. E. El absceso cerebral, metastásico del origen otico y sinusal, *Rev med latino-am* **23** 1373 (Sept.) 1938.

103 Kepes, P. Rindenabszess des Schläfelappens im Anschluss an rhinogene Meningitis, *Acta oto-laryng* **27** 165, 1939.

autopsy showed diffuse purulent meningitis by extension from the sinuses, with the cortical abscess a secondary complication. The difficulty in this case was due to the fact that cortical or subdural abscess is hard to diagnose or differentiate from meningitis if sufficient time is not available for adequate bacteriologic studies.

Kessler and Savitsky¹⁰⁴ find the Ayala index of value in the diagnosis of an abscess of the brain. This is computed by dividing the final pressure (spinal fluid) by the initial pressure multiplied by the amount of fluid removed (10 cc). If the result is over 6 it speaks against an abscess of the brain. Among 11 cases of verified abscess of the brain there was only 1 in which the index was over 5. In 1 case the diagnosis was corroborated by an encephalogram.

Richter¹⁰⁵ cites 4 cases in which the presence of meningeal symptoms offered difficulties in diagnosis, their origin being obscure. One patient, a man of 28, who had had a bilateral operation on the frontal and maxillary sinus as well as a bilateral mastoid operation, in 1935, presented himself with headache, vomiting and diplopia. Head movements were restricted, the temperature was 39.5 C (103 F), the drums and mastoids were without reaction, and only a moderate amount of mucus was present in the nose. The frontal sinuses and the antrums gave negative results on irrigation, but there was a stiff neck. The fundi were normal. Lumbar puncture yielded only three cells, but the pressure was up to 270 mm. After a few days of palliative treatment it was discovered that the patient was having only an attack of grip, falsifying his temperature. The stiff neck was due to occipital neuralgia and the paresis of the external rectus muscle had nothing to do with the case. In another patient having definite frontal sinusitis, meningitis developed, which yielded to automeningococcic serum after an operation on the frontal sinus had failed to help the patient. The author quotes Burger in the Denker-Kahler "Handbuch" on the probability of epidemic meningitis finding an atrium via an infected sinus.

Goodyear¹⁰⁶ believes that no good can come from too early intervention in meningitis suspected of being of sinus origin, at least in the stage before nature has set up any barrier. Since the spread to the meninges from the sinuses may be extremely rapid, it is important to watch patients with acute and subacute sinusitis closely for symptoms

104 Kessler, M. M., and Savitsky, N. Otitic and Sphenoiditic Hydrocephalus. The Value of the Ayala Index, *J. Mt. Sinai Hosp.* 5:486 (Nov-Dec) 1938.

105 Richter, H. Zur Differentialdiagnose otogener und rhinogener Meningitiden, *Monatsschr. f. Ohrenh.* 73:501 (Aug) 1939.

106 Goodyear, H. M. The Indication for Surgery in Meningitis Secondary to Disease of the Middle Ear and of the Nasal Sinuses. Reservations in Early Surgical Intervention, *Laryngoscope* 49:102 (Feb) 1939.

possibly indicating retention and to overcome the obstructions to drainage before extension to the meninges has taken place

Olaisson¹⁰⁷ reports a case of cured rhinogenic meningitis in a girl of 11. The disease followed acute coryza and sore throat with headaches, swollen periorbital, photophobia and rigid neck. The spinal fluid, under normal pressure, showed 496 cells, and the Pandy and Nonne tests were positive. Both antrums were cloudy. Because of the orbital swelling the author opened the ethmoid externally and evacuated a spoonful of creamy pus containing diplococci and streptococci. Local heat and methenamine were administered, and within three days the meningeal symptoms subsided. The smears and cultures from the spinal fluid were negative.

(To Be Concluded)

25 E Washington Street

107 Olaisson F. A Case of Cured Rhinogenous Meningitis. *Acta oto-laryng* 27 172, 1939

Abstracts from Current Literature

Ear

DISEASES OF THE EAR IN CHILDREN HORACE JAMES WILLIAMS, J A M A
113 990 (Sept 9) 1939

Williams discusses in full the important points in the diagnosis of the catarrhal and suppurative diseases of the middle ear, with emphasis on the anatomic variations of the ear and eustachian tube in infants and children up to 2 years of age. The genesis of infection is outlined, and the varying febrile courses associated with infections of the upper respiratory tract and acute infectious diseases such as scarlet fever and measles are clearly brought out.

Early performance of myringotomy when the indications warrant this procedure is advocated. A search of the records of 14,733 patients in the author's service at the Philadelphia Hospital for Contagious Diseases proves the truth of his plea that many untoward aural complications requiring surgical intervention were prevented by myringotomy. Mild suction with a rubber catheter hastened the removal of mucopus from the nasopharynx in many children.

In a few cases, sulfanilamide was given, but the otorrhea in these cases did not show any greater tendency to cessation than in the controls.

In the group of 1,535 patients with scarlet fever in whom suppurative otitis media developed, 35 per cent had had their tonsils and adenoid masses removed. Williams concludes as follows: 1. The structure of the infant's ear predisposes to otitis media. 2. Sinusitis is a large factor in the production of otitis media. 3. Early myringotomy is a distinct advantage. 4. Impairment of hearing should be recognized and treated early.

GORDON, Philadelphia

THE SYNDROME OF VESTIBULAR PARALYSIS IN MAN PAUL M. LEVIN, J Nerv
& Ment Dis 89 335 (March) 1939

The vestibule serves to initiate reflexes for righting and maintaining posture and for the ocular movements which compensate for movements of the head. Loss of these reflexes therefore produces a staggering gait and inability to right the body when it is dropped or placed in water. In addition, ocular fixation is not maintained during movements of the head. Levin illustrates this syndrome with the case of a man who at the age of 19 began to stagger in the dark, a symptom which grew progressively worse until he fell even in the light. A year later he lost his sense of direction in the dark or when swimming under water with his eyes closed. Two years later movements of his head caused objects about him to seem to jump. There had never been any vertigo or deafness. Neurologic examination at the age of 27 showed an ataxic gait, especially with the eyes closed, and a strongly positive Romberg sign. There was no response to the caloric vestibular tests, but a normal response of the eyes to galvanic stimuli over the ears was elicited. There was no nystagmus and no adiadochokinesia, tremor or past pointing. There was no ataxia in movements of the extremities. The remainder of the neurologic examination gave normal results, as did all laboratory tests, including those on the cerebrospinal fluid. Levin believes that this patient presented in full the syndrome of vestibular paralysis, due apparently to selective degeneration of the vestibular apparatus, but seemingly not of the vestibular nerve.

MACKAY, Chicago [ARCH NEUROL & PSYCHIAT]

DISCUSSION ON INTERNAL-EAR DEAFNESS, Proc Roy Soc Med 32 487 (March) 1939

F. W. Watkyn-Thomas first outlined the differential diagnosis of internal ear deafness from lesions of the nerve trunk and those of the middle ear. He empha-

sized that an obstructed eustachian tube with an impressed tympanic membrane can produce many of the signs of internal ear deafness. The careful analyzing of the results of the air and bone conduction tests was also emphasized. In discussing the cause of internal ear deafness he considered the bloodstream, the endolymph and the perilymph. Changes in any of these circulating fluids may affect the nerve supply of the organ of Corti. Toxins produced by focal lesions, he said, are important as a cause, and he advocated a careful search for, and elimination of, such lesions. Syphilis was mentioned as a rather uncommon cause, and pyogenic infections in the ear and nose were discussed as causative factors. Under the heading of treatment of internal ear deafness were mentioned (1) removal of foci of infection (most common in the teeth), (2) faradism and vibromassage, (3) protection from noise, (4) improvement of general health, (5) administration of vitamin B and (6) the use of hearing aids.

Suggitt showed and discussed a number of audiograms representing different types of internal ear deafness

CAMPBELL, Philadelphia

THE ELECTRICAL ACTIVITY OF A DENERVATED EAR. A. F. RAWDON-SMITH and J. E. HAWKINS JR., *Proc Roy Soc Med* **32** 496 (March) 1939

"The electrical response from the cochlea of a cat which had previously been denervated by intracranial crushing of the auditory nerve was submitted to a lengthy study, the results of which may be summarized as follows:

"The responses to acoustical stimulation derived from electrodes placed on the round window margin and in the chin muscles were studied by means of an amplifier and cathode ray oscillograph, in the usual way. Transient stimuli whose polarity could be reversed were employed to demonstrate the absence of any electrical component of neural origin such as is invariably present in a normal ear. In all other respects, however, the responses were unaffected, and both threshold contours (the so-called 'electrical audiogram') and equal response contours for approximately pure-tone stimuli demonstrated close comparability with those for normal ears. Harmonic analysis of the cochlear response yielded results departing from the normal only in such respects as would be expected in view of the complete absence of nervous component in the analysed wave.

"From these data, it is argued that this animal presented a case in which normal electrical responses were obtained from the peripheral organ, despite virtually complete degeneration of the auditory nerve, and, it follows, complete unilateral deafness. Subsequent histological examination confirmed these observations, and it is urged, therefore, that the validity of the view that the cochlear response provides an index of the hearing ability of an animal, as is sometimes stated, is open to question. Additionally, this experiment finally discredits the hypothesis that the cochlear response itself is, in any sense, neural in origin, it further indicates the necessity for caution in the interpretation of results obtained from normal ears, where the cochlear response, however derived, is in some degree, adulterated by the simultaneous presence of an action potential component."

CAMPBELL, Philadelphia

TWO CASES OF VERTIGO TREATED BY INTRATYMPANIC INJECTION OF ALCOHOL. W. S. THACKER NEVILLE, *Proc Roy Soc Med* **32** 841 (May) 1939

A patient aged 48 and another aged 55 years, complaining of deafness and tinnitus in one ear, received 3 minims (0.18 cc.) of alcohol in the labyrinth via the tympanic membrane and the foramen ovale. Both patients showed the typical vestibular reaction of a destroyed labyrinth together with complete deafness of the affected ear. The end results were not reported.

CAMPBELL, Philadelphia

THREE TEMPORAL BONES TO ILLUSTRATE THE ANATOMY OF TRANS-LABYRINTHINE DRAINAGE OF THE MENINGES AND VESTIBULOTOMY E D D DAVIS, *Proc Roy Soc Med* **32** 842 (May) 1939

The specimens showed the vestibule and external semicircular canal which had been opened, as well as the internal auditory meatus. The author remarked that he had had only about 2 successes in about a dozen cases of meningeal infection.

In the discussion Eric Watson-Williams, Watkyn-Thomas and Sydney Scott cited cases of their own and gave opinions regarding such aspects of the problem as the procedure and the development of paralysis of the facial nerve.

CAMPBELL, Philadelphia

MASTOIDITIS AND CHRONIC OSTEOMYELITIS ON THE RIGHT SIDE, PROVOKING REPEATED ATTACKS OF MENINGITIS F Ody, *Rev d'oto-neuro-ophth* **17** 164 (March) 1939

Ody reports a case of acute meningitis and petrositis, with sequester formation, in a man aged 39 years. At the age of 2 years he had had an attack of acute mastoiditis on the right side and was treated by antrotomy. In 1912 he suffered from lancinating pains in the same mastoid process. In 1920 he had headache, vertigo, vomiting and falling to the left, he was given antisyphilitic treatment. In 1934 an attack of acute meningitis occurred, and pneumococci were found in the spinal fluid. In May 1935 there developed another attack of meningitis, and the right mastoid process was everted. In November 1935 another attack of meningitis occurred, and in December still another. Roentgenograms revealed osteomyelitis and sclerosis of the petrous bone, with sequester formation. In February 1936 three operations on the petrous bone were undertaken, and part of the necrotic bone was removed, a sequester within the dura being left. The patient made a prompt recovery. A lumbar puncture made in June yielded fluid with a normal formula. In February 1939 the patient was still in good health. The presence of osteitis on the posterosuperior surface of the petrous pyramid indicated that the meningeal infection was transmitted via the vestibular aqueduct. The persistence of almost normal hearing and of part of the labyrinthine function on the diseased side suggests that the infection was propagated not by the internal ear, but by the venous channels of the bone.

DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

CENTRAL VESTIBULAR SYMPTOMS FOLLOWING DIPHTHERITIC ANGINA R MAIOU, *Rev d'oto-neuro-ophth* **17** 426 (June) 1939

Four days after an attack of diphtheria there occurred paralysis of the palate, limbs and accommodation, accompanied by slight vertigo. The vertiginous sensations continued and were increased by movements of the head, especially inclination to the right. There followed incoordination of the limbs on the right side, disturbance of deep sensibility, paralysis of the right external rectus muscle and the right twelfth nerve and spontaneous nystagmus on looking to the right, sometimes becoming pendular. There was marked disturbance of equilibrium. A caloric test revealed normal nystagmus but no vertigo.

This observation demonstrates the possibility of the existence of central lesions in the course of diphtheria. The homolateral character of the disturbance of deep sensibility indicated the presence of a low bulbar lesion. Usually, vasodilatation caused by the toxin of diphtheria is transitory, but when the intoxication is intense hemorrhagic suffusions, or even true hemorrhages, in the sheaths of the vessels are produced. This probably occurred in the present case and explains the persistence of the symptoms for seven years.

DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

PETROSITIS P C GERLINS, *Nederl tijdschr v geneesk* **83** 504 (Feb 4) 1939

By the term "petrositis" Gerlings indicates an inflammation of the cells of the petrous pyramid, the petrosal portion of the temporal bone. He describes the normal and the pathologic types of pneumatization of this area. He calls attention to the studies of Lange and Marx, which show the importance of petrositis in otogenous intracranial involvement. For the diagnosis roentgen examination is indispensable. With regard to the treatment of petrositis the various operations on the petrosal apex are pointed out. The clinical record of a boy of 8 years with petrositis is communicated, with a report of the microscopic examination of the temporal bone.

VAN CREVELD, Amsterdam, Netherlands [AM J DIS CHILD]

Pharynx

SWELLING OF THE PALATE IN A WOMAN AGED FORTY-NINE R R SIMPSON, *Proc Roy Soc Med* **32** 1237 (Aug) 1939

This patient showed a large, smooth cystic swelling of the whole palate, except the posterior half of the soft palate. The nature of the condition was doubtful, and guidance was sought as to the best method of handling it.

CAMPBELL, Philadelphia

PLAUT-VINCENT INFECTION ON THE BASE OF TONGUE AND EPIGLOTTIS F IPOLYI, *Monatschr f Ohrenh* **73** 647 (Oct) 1939

In connection with a case of Plaut-Vincent angina involving the vallecula and the epiglottis, the possible complications of this disease are discussed. The treatment employed consists of painting the ulcerations with a 1 per cent solution of acriflavine hydrochloride and the use of a diluted gargle of the same substance.

LEDERER, Chicago

CLINICAL AND ROENTGENOLOGIC EXAMINATION OF THE NASOPHARYNX HEINZ G A BAYER, *Ztschr f Hals-, Nasen- u Ohrenh* **45** 247, 1939

After discussing the various methods employed in the roentgen examination of the nasopharynx, Bayer describes his personal technic. He uses either stereoscopic or serial roentgenograms, a distance of 70 cm, 70 kilovolts, 150 milliamperes, 0.4 to 0.6 second. By this method, he can outline the various landmarks and particularly stress the study of the soft tissues of the nasopharynx and their relation to the spine and cranium. He then presents several cases of pharyngeal growths (adenoids, tumor, angiofibroma), which can readily be diagnosed through his technic.

The second portion of his paper is a practical consideration of his particular roentgen technic, as particularly applied to an adenoidectomy. He feels that, owing to improper position of the head, injury to the atlantis protuberance, the sphenoid body and the basilar portion of the occipital bone can occur easily. He advocates a slightly forward flexion of the head as the proper position to be used.

PERSKY, Philadelphia

Larynx

CARDIOSPASM O STANLEY HILLMAN, *Proc Roy Soc Med* **32** 1235 (Aug) 1939

Hillman reports a case of cardiospasm in a man of 44 years on whom sympathectomy was performed, the stomach was opened and the cardiac orifice dilated with the fingers. Recovery was uneventful, and relief of the dysphagia was obtained.

In the discussion V E Negus commented on the fact that a better result was produced by digital stretching than was obtained by dilation through an esophagoscope. He said he believed it was because the abdominal surgeon straightened as well as dilated the esophagus.

CAMPBELL, Philadelphia

LARYNGITIS TUBERCULOUS? E WATSON-WILLIAMS, *Proc Roy Soc Med* **32** 1236 (Aug) 1939

The larynx of this patient who showed roentgenographic evidence of active tuberculosis of the lungs, revealed red and dry vocal cords without edema or ulceration. It was doubtful if a tuberculous lesion was present in the larynx.

CAMPBELL, Philadelphia

RESULTS OF EMERGENCY TRACHEOTOMY FOR FOREIGN BODY OF THE AIR PASSAGES IN CHILDREN. TWO CLINICAL CASES. A LAMBESCU, *Med inf, Rumania* **1** 166 (March-April) 1939

Lambescue, after classifying the solid foreign bodies that may fall into the larynx and tracheal tube, explains the symptomatic picture and the elements of diagnosis. The discussion of the treatment occupies the greatest place and is directed first toward the extremely dramatic situation in which one is obliged without hesitation to practice tracheotomy as an emergency measure and second to the situation less pressing in which it is convenient to resort to a tracheo-bronchoscopic procedure. In order to avoid complications, one should not neglect any details of technique.

By means of tracheotomy, the author has saved 2 children with obstruction of their respiratory paths. If the foreign body is not embedded, one can replace the bronchoscopic approach with tracheotomy when one does not have access to a bronchoscope or to a specialist in this form of practice. It is the method to be preferred when asphyxia is acute. At other times tracheotomy should be the preliminary procedure. For children the operation of choice should be high tracheotomy under local anesthesia.

FROM THE AUTHOR'S SUMMARY [AM J DIS CHILD]

Miscellaneous

THE CHEMOTHERAPY OF EXPERIMENTAL TYPE II PNEUMOCOCCIC MENINGITIS. PAUL GROSS and FRANK B COOPER, *Am J M Sc* **97** 609 (May) 1939

Gross and Cooper produced infection of the meninges in a group of 54 rats with a 1:100,000 dilution of a culture of a type II pneumococcus, corresponding to about ten fatal doses. The fatality rate was 100 per cent in the control group (20 animals) and 60 per cent in the sulfone group (15 animals), the sulfanilamide-treated group (15 animals) showed a fatality rate of only 26.7 per cent. The initial treatments were begun six hours after the infection. A series of 45 rats were infected with a 1:10,000 dilution of the same culture, corresponding to about one hundred fatal doses. All control animals (15) were dead within sixty-eight hours, and all but 1 of the 15 sulfone-treated rats within forty-four hours. The sulfanilamide group (15 rats) showed a survival rate of 46.7 per cent, with an average survival time of one hundred and thirty-three hours for the rats which died. Treatments similar to those in the first experiment were initiated six hours after the infection. Within less than twenty hours, 6 control and 3 sulfone-treated rats had died, they showed extensive and diffuse, but not uniformly distributed, purulent leptomeningitis of the brain and spinal cord. Sulfanilamide is suggested as an adjuvant of specific serum therapy, or as the primary therapeutic agent when such serum is not available, as a means toward an effectively lowered mortality rate for pneumococcic pneumonia and meningitis in man.

MICHAELS, Boston [ARCH NEUROL & PSYCHIAT]

PARALLEL STUDY OF THE PATHOGENESIS OF RHINOCENOUS OPTIC NEURITIS AND OF SEROUS IRITIS B WALDMANN, *Am J Ophth* **22** 44 (Jan) 1939

Waldmann cites several cases of neuritis and iritis, evidently due to sinus infection. He discusses their pathogenesis and gives the following summary:

"As can be seen from the foregoing, the pathogenesis of optic neuritis and of serous iritis displays considerable differences, they have, however, many points in common.

"The optic neuritis or rhinogenic origin is the outcome of an aseptic process going on in the optic canal, and is brought about exclusively by mechanical factors. Its origin is in the empyema of the posterior sinuses, or the chronic hypertrophic inflammation of the latter.

"Spontaneous serous iritis, even in the presence of syphilis or tuberculosis, is in every instance the outcome of a catarrhal infection.

"The source of infection is the catarrhal inflammation of the posterior sinuses, and pathogenic agents migrate directly from the sinus into the canal and thence, by way of the pia mater, into the uvea." W S REESE [*ARCH OPHTH*]

MENINGIOMAS OF THE BRAIN G HORRAN, *Arch Neurol & Psychiat* **41** 140 (Jan) 1939

The sections of this review on meningiomas arising from the olfactory groove and on orbital temporal meningiomas are of special interest to the ophthalmologist. The first type of meningioma results in atrophy of the optic nerve together with loss of olfactory sense on the same side, mental change and finally increased intracranial pressure and choking of the optic disk on the uninvolved side. The second type results in marked and gradually increasing protrusion of one eye due to the enormous bony thickening of the orbital roof and of the bone lateral to and beneath the orbit in the region of the sphenoid ridge, together with invasion of the orbit posteriorly by the tumor, which has extended through the bone from its intracranial origin.

R IRVINE, Los Angeles [*ARCH OPHTH*]

TORTICOLLIS SPASTICA OLAN R HYNDMAN, *Arch Otolaryng* **29** 927 (June) 1939

Hyndman reports 3 cases of spastic torticollis, in all of which the patient reacted strongly in Barany tests. In 1 case relaxation of the spastic muscles was noted when the patient was reclining or when the head was tilted backward. In a case of spastic torticollis of seven years' duration, the spasmodic jerks of the head ceased completely when a cold caloric test was made on the left ear, and gradually returned after the induced nystagmus ceased. The spasmodic jerking of the head disappeared also when the right ear was irrigated with cold water. With the hot caloric stimulus the tendency for the spasmodic jerking to stop was much less striking than with the cold caloric stimulus. Severe stimulation of other parts of the body increased the torticollis. To eliminate the possibility of suggestion, the patient was informed that a test would be made as usual, but the water injected was at body temperature. The torticollis was not influenced. An acid ash diet with ammonia chloride was tried with benefit, after which it was decided to section the right vestibular nerve. The torticollis disappeared for ten days, but reappeared on the eleventh day. Three weeks after operation, a cold caloric stimulus was applied to the right ear to test the adequacy of the section of the vestibular nerve. The test had a mild and transitory influence on the torticollis. Auditory tests showed complete absence of audition on the side of the operation. During the ensuing four months the patient did not experience Meniere attacks of dizziness, but the torticollis was the same as before operation. Four months later the remainder of the eighth nerve was sectioned, without influence on the existing spontaneous cerebellar nystagmus. On the third postoperative day the

torticollar twitches appeared. Two weeks later a cold caloric test on the right ear showed no reaction and had no influence on the torticollis. Five months after the second and four months after the first operation, cervical laminectomy with bilateral section of the first, the second and the third anterior root and of the spinal accessory nerve was done. Fifteen days after discharge the spasms returned, but to a much less degree, indicating that, although the vestibular apparatus is involved in certain cases of spasmodic torticollis, destruction of the end organ in this case failed to abolish the torticollis permanently and that the locus operandi is central.

HUNTEI, Philadelphia [ARCH NEUROL & PSYCHIAT]

SERUM THERAPY OF STREPTOCOCCIC INFECTION OF THE NOSE, THROAT AND EAR AND ITS COMPLICATIONS A. E. SHEPIAR, M. J. SPENCE and W. J. MACNEAL, Arch Surg **38** 206 (Feb.) 1939

Additional reports are given on 30 patients suffering from severe infection with hemolytic streptococci in the field of otolaryngology, 4 with complicating meningitis and 15 with blood yielding bacteria on culture. These patients were treated with streptococcus serum of three different kinds. In some instances other therapeutic procedures were used along with the injection of serum. There were 7 deaths in this group. The authors conclude that the early use of chemotherapeutic and biologic agents for the control of infections with hemolytic streptococci may be expected to reduce appreciably the need for operative procedures.

KAISER, Rochester, N. Y. [AM J DIS CHILD]

ORAL ADMINISTRATION OF RAGWEED POLLEN J. H. BLACK, J. Allergy **10** 156 (Jan.) 1939

Black has treated hay fever by oral therapy for a number of years in a gradually decreasing number of patients. He tried it again on 40 patients during the ragweed season of 1938. He concluded "Oral therapy with ragweed pollen gives perfectly satisfactory results in some patients and fair results in a larger group, but does not compare favorably with the results obtained by hypodermic treatment. In three patients it was found that the oral administration of pollen made it possible to increase the hypodermic treatment much more rapidly than could be done before pollen was administered by mouth."

HOYER, Cincinnati [AM J DIS CHILD]

ROLE OF HEREDITY IN STUTTERING S. E. NELSON, J. Pediat **14** 642 (May) 1939

Nelson compared the lineage histories of 204 stutterers with those of 204 non-stutterers. The subjects of both groups were matched in age and sex. Those belonging to the stuttering group were selected only because they stuttered, those belonging to the control group were selected because they spoke normally and had no history of stuttering. Additional information was secured from grandparents, aunts, uncles and friends. The trend of the data seems definitely to indicate that there must be some biologic tendency to stutter. The conclusions pointing to that tendency are as follows. A greater percentage of stutterers who have ancestral pedigrees of stuttering began to stutter when they were learning to speak, while a greater percentage of the stutterers whose pedigrees show no ancestral stuttering began to stutter after the onset of speech. There is a constant ratio in favor of the greater incidence of diseases and other precipitating factors occurring at the onset of stuttering among stutterers whose pedigrees show no ancestral stuttering than among stutterers whose pedigrees show ancestral stuttering. Many of the stutterers with pedigrees of ancestral stuttering show a history of no diseases or other precipitating factors coincident with the onset of speech and stuttering, as compared with the percentage of stutterers with pedigrees with

no ancestral stuttering. The manner and character of the accidents, frights and diseases are more violent and more severe among those stutterers having pedigrees of no stuttering than among stutterers showing stuttering in their ancestry.

J A M A

TREATMENT OF THE COMMON COLD IN INFANTS AND CHILDREN. R. L. J. KENNEDY, Minnesota Med 22 1 (Jan) 1939

Under the term 'common cold' Kennedy includes acute inflammation of any or all portions of the upper part of the respiratory tract. He feels that the cause may be a filtrable virus with bacteria as coincidental or secondary invaders. He advises isolation of infants from infected persons. Treatment may be preventive or symptomatic. Vaccine may be given with the understanding that although not harmful, it may not prove beneficial. Kennedy feels that proof is lacking that there is any substance in food or in preparations of vitamins which specifically prevents colds. For treatment he advises rest in bed, sedatives, humidity, baths, antipyretics and occasionally the use of epinephrine or ephedrine as nasal drops or a spray.

ANDERSON, Minneapolis [AM J Dis Child]

BRONCHOSCOPIC DILATATION OF BRONCHIAL STENOSIS FOLLOWING THORACOPLASTY FOR TUBERCULOSIS. EDWARD B. BENEDICT, New England J Med 220 617 (April 13) 1939

Bronchoscopic intervention is as important for the relief of bronchial stenosis due to tuberculosis as for any pathologic condition causing stenosis. As yet it cannot be said that stenosis follows thoracoplastic procedure.

Benedict feels that some tuberculous tracheobronchitis probably exists before the procedure is done. This procedure however may activate the process simply by compression and approximation of the bronchial surfaces. Because of this suspicion of preexisting tracheobronchitis it is important to use bronchoscopic procedure as a preliminary to collapse therapy. Three cases of the stenotic type of tuberculous bronchitis are reported in all of which great benefit was obtained by the use of the bronchoscope. In no case did the procedure reactivate the tuberculosis.

SCHALL, Boston

MIGRAINE: A PITUITARY STUDY. R. O. HALLORAN, West Virginia M J 35 233 (May) 1939

Halloran proposes that migraine is due to swelling of the pituitary gland, which creates compression of the cavernous sinuses resulting in congestion of the whole venous system of the skull. Pressure on the pain papillae within the walls of the dural sinuses creates the headache. The various components of migraine are thought to be pressure phenomena having their origin in the nerve structures and about the cavernous sinuses and the sella turcica. It is further proposed that ergotamine tartrate (gynergen) decreases the vascular bed of the skull and brain which in turn relieves the congestion and headache. The depression following migraine is thought to be due to accumulation of metabolites in the sensorium. Thus many mental states may be due to anoxemia of the brain. Further studies are indicated in the use of ergotamine tartrate and oxygen in the treatment of mental states such as acute alcoholism and cerium tremens. A close analogy of migraine, epilepsy and epilepsy is suggested. The periodic attacks of migraine are in keeping with the periodic function of the pituitary gland. There are many cases of migraine due to allergy. The author believes that explanation of this may lie in the fact that the anterior lobe of the pituitary gland is derived from the pouch of Rathke from which the nasal process is derived. The latter is allergic. Hence it is not unlikely that the anterior lobe is an allergic shock tissue and responds to allergy by swelling.

J A M A

THE TREATMENT OF DYSPHONIA AND ALLIED CONDITIONS CORTLANDT
MACMAHON, J Laryng & Otol 54 343 (June) 1939

Dysphonia occurs as a result of some operations on the throat and larynx and may also be due to infection of the cords by toxins from the antrums, teeth, tonsils and nasopharynx. Certain heart ailments and severe illnesses produce a weakness of the voice. It is often caused by gross misuse of the voice.

Professional users of the voice should learn something about correct voice production, to the benefit of themselves and their auditors. Short vocal rest following medical attention, as well as correct breathing, especially nasal breathing, and a healthy membrane of the nose are essential for restitution of a normal voice which has become impaired.

The first thing in voice culture is to acquire lower costal breathing. This produces a deeper vocal pitch. The deep pitch is helped enormously by driving the tongue back with a tongue depressor on the sound of "ah."

After operations for cancer and papillomas the same treatment is followed. A misused voice responds quickly to such treatments. Often the cause of misuse is overbreathing. This must also be corrected.

In the treatment of functional aphonia the patient sits in a chair with the mouth widely opened. The middle finger of the physician's right hand depresses the tongue, overcoming any possible resistance. The fingers of the left hand are placed on the posterior edges of the thyroid cartilage. The patient is then asked to cough. If the cough is strong he is asked to cough again and finish the cough on the sound of "ah." This often is followed by voice production. Sometimes several treatments are necessary.

Spastic dysphonia usually occurs in professional voice users of nervous temperament. It is rare. The patient must first acquire a feeling of repose. The voice must be trained to produce a low pitch. The sternohyoid and the omohyoid muscles are made to contract. Development of these muscles helps to overcome the spasticity.

After laryngectomy, the new abdominal voice should be tried soon, even before healing is complete. The patient is shown how to get air into the stomach by swallowing it and then how to sound vowels on top of the belch. It is a mistake to attempt the acquisition of the pharyngeal voice while using an artificial larynx. The effort to attain a pharyngeal voice should be encouraged, and if it is impossible for the patient to acquire it the artificial larynx may be prescribed.

LE JEUNE AND BAYON, New Orleans

RIGHT HEMIANOPIA PERSISTING FIFTEEN YEARS AFTER CEREBRAL ABSCESS
SYDNEY SCOTT, Proc Roy Soc Med 32 512 (March) 1939

A man was operated on for an otitic-temporosphenoïd abscess on the left side in July 1923 and recovered except for restriction in the fields of vision. The macula escaped, and the patient has been able to carry on his profession without great inconvenience.

CAMPBELL, Philadelphia

COLORED AUDITION H PROBY, Rev d'oto-neuro-opht 17 261 (April) 1939

The phenomena that constitute colored audition arise in the domain of vision and are provoked by sensations or ideas outside the ordinary laws of perception. They are simple luminous or colored impressions, symbols, diagrams or even persons, of variable intensity, or they may be merely an abstract notion of color. Colored audition (*synopsies*) is slightly more frequent in women; it may be acquired through examination which calls the patient's attention to the phenomenon, or it may be spontaneous. It is usually lasting, and while the manifestations may be diminished in frequency or intensity by age, they persist and are rarely modified. Colored audition arises frequently in young persons. Whether it occurs in youth or later as a result of external influences, a favorable terrain, prepared by heredity, is implied. Identical formulas are rare, although Lemaitre reported the instance of a mother and child, in each of whom the vowels produced

the sensation of the same colors The study of colored audition in identical twins would shed additional light on the factor of heredity Colored audition is not pathologic, but is found only in normal persons

DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

RELATION OF MIGRAINE AND NEURALGIAS OF THE FACE J HAGUENAU and H KAUFMANN, *Rev d'oto-neuro-opht* **17** 321 (May) 1939

Certain neuralgias, so-called migraine neuralgias, are distinct from tic douloureux and constitute the equivalent of migraine In "migraine neuralgia" the area of the pain and cutaneous hyperesthesia is not strictly limited to the distribution of one branch of the fifth nerve but encroaches on the field of several branches, and sensorial excitations and meteorologic changes affect the sufferers more easily than they do persons with essential neuralgia Migraine neuralgias are distinguished from other sympathalgias by not being continuous, by affecting especially females and sufferers from long-standing migraine and by their evolution Like migraine, they tend to react to episodes of the sexual life, appearing at the menstrual period or at the beginning of the menstrual cycle, disappearing during pregnancy or amenorrhea and being modified by the menopause Like migraine also the attacks are sometimes almost continuous, or they may disappear over a long period or alternate with crises of migraine They are not cured by injection of alcohol into the nerve This is the only type of neuralgia of the face that is akin to migraine

DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

ABSCCESS OF THE RIGHT FRONTAL LOBE REVEALED BY TRAUMA OF THE LEFT ORBIT A BARRAUX, P ROQUES and J E CAMBASSEDES, *Rev d'oto-neuro-opht* **17** 336 (May) 1939

The authors report the case of a man aged 22 years who experienced headache, vertigo and bradycardia after a fall and a blow to the region of the left orbit The spinal fluid was slightly tinged with blood Roentgenographic examination revealed no evidence of fracture and very slight clouding of the right nasal sinuses After several episodes of return of the headache and bradycardia, each time relieved by spinal puncture, emphoria developed, and the patient escaped from the hospital The morning after his leaving the hospital he suddenly fainted and died within a few minutes There had been no rise of temperature and no neurologic signs except paresis of the left sixth nerve and bilateral papillary stasis, which developed shortly before death Autopsy revealed a fracture of the roof of the left orbit, at which point the congested frontal lobe was adherent The right frontal lobe was increased in volume, was not adherent and contained a large abscess with a thick capsule The cortex and ventricles were normal Inquiry revealed that the patient had complained for a long time before the accident of rhinorrhea, accompanied by intermittent headaches in the right frontal region It was also learned that at the time of the accident the patient had been wounded in the left orbital region by a blow from a bayonet during a friendly scuffle The authors believe that the abscess was secondary to the low grade sinusal infection and had developed over several months, giving time for formation of the capsule The trauma was regarded as an important contributory factor in that it upset the cytoarchitectonics and myeloarchitectonics in a region rendered vulnerable by the presence of the abscess

DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

LABYRINTHINE DISTURBANCES WITH PAPILLARY EDEMA IN THE COURSE OF MYELOID LEUKEMIA R MAYOUX, *Rev d'oto-neuro-opht* **17** 346 (May) 1939

Mayoux reports the case of a woman aged 32 years who had typical myeloid leukemia, the blood contained 320,000 leukocytes per cubic millimeter, of which 44 per cent were polymorphonuclears and 14 per cent myelocytes Deafness, ver-

tigo and papillary stasis developed rapidly. There were spontaneous horizontal nystagmus to the left and no reaction to the caloric test. Two types of labyrinthine lesions are observed in the course of myeloid leukemia: hemorrhage in the labyrinth and myeloid infiltration. It may be assumed that the same type of edema existed in the labyrinth as in the eyegrounds. Myeloid infiltrations are abundant around blood vessels, often they invade the vascular lumen, causing thrombosis.

DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

TREATMENT OF POSTDIPHTHERITIC PARALYSIS WITH VITAMIN B₁ P. FEIGE, *Fortschr d Therap* **15** 333 (June) 1939

Reviewing 1,590 cases of diphtheria which were observed during the years 1936 and 1937, Feige found 100 cases in which postdiphtheritic paralysis developed. Paresis of the soft palate was observed in 90 cases, paresis of the ocular muscles in 20 cases, paralytic symptoms of the legs in 23 cases, paralysis of the pharyngeal muscles in 18 cases, paralysis of the respiratory musculature in 4 cases, paralysis of the musculature of the neck and back in 3 cases and paralysis of the diaphragm only once. Some of the children had more than one form of paralytic symptoms, and in 18 cases the paralysis threatened life. Of the 60 patients in whom the entire course of the postdiphtheritic paralysis could be observed, 30 were treated with a preparation of vitamin B₁ and 30 either received no treatment for the paralytic symptoms or were treated with other medicaments. A comparison of these two groups of patients revealed that in those who were treated with vitamin B₁ the paralytic symptoms persisted on the average for twenty-nine and six-tenths days, whereas in the other group they persisted on the average for forty-nine days. The author administered the vitamin B₁ by mouth and by intramuscular injection on alternate days. On one day the children were given three times 1 tablet containing 1 mg of the vitamin, that is, 1,200 pigeon units, on the following day they were given an intramuscular injection of 1 cc of a vitamin B₁ preparation which contained 4,000 pigeon units. In discussing the pathogenesis of postdiphtheritic paralysis, the author cites observations of several investigators and suggests that these postdiphtheritic paralytic symptoms are the result of the concurrence of toxic impairment of the tissues and lack of the B₁ substance, which has a ferment-like action. He thinks that this explains at the same time the success of the treatment with vitamin B₁.

J A M A

Society Transactions

AMERICAN LARYNGOLOGICAL ASSOCIATION

JAMES A. BABBITT, M.D., *President*

WILLIAM E. GROVE, M.D., *Editor of Abstracts*

Sixty-Second Annual Congress, Rye, N. Y., May 27-29, 1940

President's Address The American Laryngologic Association Past and Future DR. JAMES A. BABBITT, Philadelphia

(The history and development of the association from its inception in 1878 to the present time were sketched. The limited membership of the association was defended, although Dr. Babbitt felt that all important sections of the country should be fairly represented. He discussed the "dignified induction" of new fellows and a "respect for tradition" among them, dwelling at length on the functions of the "candidates' nominating committee" and advocating frequent changes in its membership. The scientific contributions presented by various past presidents in their annual addresses were discussed. Dr. Babbitt presented the set-up for the annual meeting, particularly in relation to the annual meetings of other national societies in the same field, and stated the opinion that a reduction of the length of the meeting to two full days should be considered. The special funds of the association and their application to research problems were carefully considered.)

Plummer-Vinson Syndrome with Report of Esophageal Findings in Several Cases DR. JOHN D. KERNAN, New York

This article will be published in full in a later issue of the ARCHIVES

DISCUSSION

DR. CHEVALIER L. JACKSON, Philadelphia. I think the condition which Dr. Kernan has brought to attention is extremely important. I have seen it in several cases and should like to describe briefly a typical example I recently encountered.

The patient was an elderly woman with dysphagia, who was thought to have a cancer of the esophagus. I examined the roentgenograms at the hospital. The roentgenologist had not had much success in demonstrating a stenosis and was vague on the question of cancer. One glance at the patient was sufficient for me to make at least a tentative diagnosis of the so-called Plummer-Vinson syndrome. She was thin and had fissures at the corner of the mouth. Her tongue was smooth and showed typical atrophic glossitis. A typical web was found along the right lateral wall of the esophagus, which, as Dr. Kernan has pointed out, allowed the esophagoscope to pass through easily, offering no particular resistance to the instrument. Even after the passage of the instrument enough of the web remained so that it could be demonstrated on roentgenograms taken on the following day. So far I have given her just one treatment, but the improvement in swallowing was striking. She noted immediate improvement and gained 8 pounds (3.6 Kg.) in a week. She will return for another dilation in a few weeks. She had been getting iron medication from her family physician. She also had chronic anemia and hypochromemia.

My feeling in regard to this case and a number like it which I have encountered is the same as Dr. Kernan's, that the patients are not hysterical. I am

rather inclined to think that the condition is not spasmodic but that there is an organic stricture causing the dysphagia. As to whether this condition is primary or whether the anemia or some other general condition is primary I do not know.

I have never seen cancer develop in any of these cases, and I have been looking for it. Mr. Negus, of London, is strongly of the opinion that in the British Isles cancer is found in a definite percentage of cases of this kind.

Dr. Gerlings, of Amsterdam, published an article (*J. Laryng & Otol* 54 23 [Jan.] 1939) with a number of roentgenographic studies which showed fairly well the stenosis of the esophagus.

DR. LOUIS H. CLERF, Philadelphia. This subject is extremely interesting. I have had the opportunity of observing a number of cases of this kind for a considerable time, and I, too, have been unable to find carcinoma in any of them.

It is rather unfortunate that the question of hysteria and neurosis has been injected into this syndrome, because I am convinced that the disease is systemic. Food deficiency was mentioned. I have seen patients with carcinoma of the esophagus and stricture of the esophagus who were practically starved to death and yet had no evidences of atrophic changes in the mouth, fissures at the angles of the mouth or atrophic changes in the esophagus. They were simply starved. I do not think a deficiency disease in itself is the cause of this syndrome, although it may enter into the picture. Patients with the food deficiency diseases, for instance pellagra and beriberi, do not exhibit this sort of picture at all. Men suffer from food deficiency diseases as frequently as women, but this syndrome is limited exclusively to women. Therefore, I believe that it must be due to a hormone or a vitamin-hormone combination and is not simply a matter of starvation, such as the average patient with duodenal or gastric ulcer experiences.

The esophagoscopic observations also suggest that the condition is not merely a lesion at the upper end of the esophagus. True, webs are observed there, but the roentgenograms that Dr. Kernan exhibited showed changes along the full length of the esophagus. Had he used a flexible gastroscope and inspected the interior of the stomach he would have seen atrophic changes in the mucosa of the stomach also. I have seen this in 2 cases.

I think this disease is systemic. Just what it is I do not know. Of course, the outstanding symptoms are the dysphagia and the lesions in the mouth and throat.

DR. HARRIS P. MOSHER, Boston. This paper is exhaustive and judicious. It is exhaustive because it presents evidence on so many opposite and opposing sides.

I am just as dogmatic as Dr. Vinson, and I maintain that there is in a majority of these cases, at least in all the cases that I have come across, a physical basis for this disease, for instance, a web, and that treatment of the web does away with the symptoms. I have believed and still do that in 99 per cent of the cases all the symptoms naturally follow the obstruction caused by the physical web or stricture.

Now as to the examination of the esophagus, I will go on record as saying that half of the physicians who examine the esophagus do not see it. They examine it under local anesthesia with what I call pinpoint-sized tubes and they do not see what is there. That is the reason for the reports of normal observations and is the cause, in my opinion, of the failure to find the webs.

Brown-Kelly was quoted. He stated the belief that a disturbance in Auerbach's plexus as the result of infection was the cause of obstruction at the lower end of the esophagus. In his more recent articles he has admitted observing an ascending fibrosis of the terminal portion of the esophagus due to infection, and I believe that he will also change his opinion that hysteria or spasm is the cause of this so-called Plummer-Vinson syndrome.

Dr. Cordray did some experimental work on this question using rats (*Am. Otol. Rhin. & Laryng* 49 160, 1940). He worked with a sufficient number and starved the animals for a sufficient length of time, but he found no webs of the esophagus. He did find hyperplasia of the epithelium characteristic of animals fed on grain, that is, a hyperplasia of the superficial layers of the epithelium. He observed that

the basal layer of cells of the epithelium showed a change suggesting, perhaps, a precancerous lesion. In other words, it looked as though there was some deep change in the mucous membrane of these rats following the prolonged starvation. I feel that in a small number of these cases there is a dietary change which does cause this disease.

The most startling addition to general knowledge of diseases of the esophagus was made by an author in South America whose name I have forgotten. His work, done in London, proved that an enlarged esophagus with an obstruction at the lower end was due to a degeneration of Auerbach's plexus caused by food deficiency and was analogous to beriberi. I have never seen an example of this condition in this country.

Atrophic vaginitis of elderly women, which the doctor described, is common and is reported in the literature. This is a condition of the mucous membrane analogous to the conditions found in some of these cases of the so-called Plummer-Vinson syndrome.

As to the question of hysteria, any one who miss-swallows and experiences the hideous imitation of strangling which that causes would also be hysterical the next time he tried to swallow, and persons with esophageal webs do strangle, owing to an overflow into the larynx.

DR JOHN D KERNAN, New York. The most striking factor in some of these cases has been that the symptoms of dysphagia were slight, almost unnoticed. The patients feel a little miserable and state that once in a while they have slight difficulty. "I feel as though my food were not going to go down and then it does." As Dr Mosher says, when those patients are examined with the esophagoscope, one is likely to miss the condition entirely as the tube goes down, but on the way back one notices a little hemorrhage starting up. Then it is realized that something has been ruptured. It is the mild conditions which should be noticed.

An important point which I did not emphasize is that it may be dangerous to subject these patients to esophagoscopy. If the web formation or the atrophy has proceeded to any great extent, the wall is apt to be tender and easily ruptured. Esophagitis may follow the procedure, as in one of my cases.

Certain Reactions of Laryngeal Tissues to Medicinal Agents DR RALPH A FENTON, Portland, Ore

This article will be published in full in a later issue of the ARCHIVES

DISCUSSION

DR HARRIS P MOSHER, Boston. I think you realize, as I do, that this paper is a physiohistologic report on what happens with the use of certain medicaments now employed in the treatment of conditions of the larynx, and it is important from that standpoint.

I wish Dr Fenton would go further in his study and check on the glands. I have a strong feeling that the more that is known about the glands, the more will be known about the mucous membrane.

DR FRANK R SPENCER, Boulder, Colo. I have used dilute solutions of lactic acid but never a 50 per cent solution. That would be destructive. Weaker solutions, 5 to 10 per cent, cautiously applied over laryngeal ulcers often help a great deal. I have used a little trichloroacetic acid, much weaker than 50 per cent, to apply to ulcers, though in recent years I have preferred the cautery.

I hope that Dr Fenton will in some subsequent work show the reaction from weaker solutions, because as far as I know all the authors have recommended weaker solutions than 50 per cent of trichloroacetic and lactic acids.

DR RALPH A FENTON, Portland, Ore I realize, as Dr Mosher has suggested, that this study is somewhat in uncharted territory, and therefore it is undoubtedly necessary that the work will have to be augmented by the work of others who have perhaps more opportunity to do this sort of experimental work than I have I feel strongly that the work should be continued, not only to investigate the use of weaker solutions, as suggested by Dr Spencer, but particularly to see whether the initial repair continues, as I have seen it do in many months of experiments on sinusitis, using the same type of animal Young kittens are rather tender and timid, and I expect that at another time older animals may be used, with a more accurate response

But I do make a plea for the exercise of care in the inundation of the larynx with fairly strong caustic agents

Unusual Tumors of the Upper Part of the Respiratory Tract DR LE ROY A SCHALL, Boston, and DR DAVID P CORDRAY (by invitation), Boston

(This paper was a report of the unusual tumors of the upper part of the respiratory tract, with illustrative slides The series included rhabdomyosarcoma of the choanae, neurofibroma of the vocal cord, plasmocytoma of the pharynx, osteogenic sarcoma of the antrum, Ewing's tumor of the ileum with metastasis to the sphenoid, metastatic hypernephroma of the maxillary antrum and fibrosing osteitis of the antrum)

DISCUSSION

DR THOMAS E CARMODY, Denver This paper is very interesting, especially Dr Schall's slides The unusual character of these cases is something that is not commonly seen

(Dr Carmody then showed a series of slides illustrating (1) a neurofibroma of the cheek and the periosteum of the lower right jaw which recurred after removal but has not again recurred in the four years following the second removal, (2) an unusual osteogenic sarcoma of the mandible, after the removal of which a rib was employed as scaffolding, before this patient's death from an accident about two years later the rib was practically covered by a new formation of bone, (3) a soft tumor for which the diagnosis of squamous cell carcinoma had been made but which he now stated may have been a Ewing tumor [associated with destruction of ileum and femur and treated by irradiation, with but little effect], (4) an osteosarcoma of the jaw associated with an osteoma which had been previously removed [giant cell tumor in a child aged 11 or 12 years], with the surrounding areas showing evidence of osteoblastic and osteoclastic activity [treated by radium], and (5) tuberculosis of the jawbone following the extraction of a tooth)

DR JOSEPH C BECK, Chicago It is alarming to hear such a paper on the differential diagnosis of a tumor known as a plasmocytoma and also as a myeloma by the eminent pathologists Dr Schall has associated with him and by Professor Ewing and similar pathologists Clinicians must be on guard with that type of a tumor, and while the histologic changes in respect to the cytoplasm of the cell are similar, the course of the disease is different I have had a patient with this condition I have been assisted by Professor Ewing and a number of other physicians in the study of this case, and I passed around a preparation which they really could not differentiate because of the fact that there were degenerative processes present That is something I should like to have Dr Schall and any one else who discusses this paper emphasize Not only are there characteristic cellular elements in the tumors, but there are also degenerative changes which make the diagnosis difficult

I should like to refer to the case of hypernephroma The hypernephroma metastasis does not occur only in bone It has been said that it occurs mostly in bone, which is true, but there is also hypernephroma of the larynx An interesting paper has recently been published in a French journal, but I cannot recall the author's name It brought up the questions as to whether there were laryngeal symptoms far ahead of anything referable to the kidney and whether there was such a thing as primary hypernephroma of the larynx

DR ERNEST M SEYDELL, Wichita, Kan I should like to report a case of leiomyoma myxosarcoma of the orbit which I observed at the University of Illinois last year at the board examinations This case was diagnosed by Dr Brunner, who stated that only 3 or 4 cases had been reported in the literature I thought it would be interesting to add to the record

Laryngeal Stenosis Report of a Case DR CHARLES J IMPERATORI, New York

This is a further report on a patient presented before the American Laryngological Association last year (ARCH OTOLARYNG 30 841 [Nov] 1939) A short summary of the case is necessary so that a proper continuity may be established

This young man has laryngeal stenosis due originally to multiple papilloma Attempts to treat this condition resulted in a complete stenosis, induced by radium therapy externally and internally and by two laryngostomies When he was presented last year, he had a no 38 core mold within his larynx, and on removal of this dilator his larynx would immediately contract After his presentation it was decided to use a smaller core mold, and a no 26 was used up until the middle of November 1939 It was then found that he would tolerate the removal of the core mold with very little contraction and closure of the tracheotomy opening It was necessary to replace the core mold from time to time until the first week of April of this year, but since that time, he has worn neither the dilator nor the tracheotomy tube The tracheal stoma has been kept closed by adhesive plaster and a bandage During the past year, he has worn a core mold for 229 days

The important point that should be stressed in dilation of the larynx is to not overdilate it and to promote epithelization

The tracheal stoma will not be closed in this man until it is definitely certain that the laryngeal lumen will remain patent and of sufficient size

Plastic Closure of a Tracheoesophageal Fistula Report of a Case DR CHARLES J IMPERATORI, New York

This is a further presentation of Master Robert Sippel, the son of Dr R L Sippel, who was presented last year with complete cure following the closure of a tracheoesophageal fistula (ARCH OTOLARYNG 30 352 [Sept] 1939) The condition is entirely cured, although the patient occasionally has regurgitation of food, undoubtedly due to a spastic condition of his cardia

Dr Porter Vinson (The Diagnosis and Treatment of Diseases of the Esophagus, Springfield, Ill, Charles C Thomas, Publisher, 1939) described the phenomenon that occurred in this child following the swallowing of a string, and the illustration (p 11) is self explanatory

In order that his cardiac spasm could be dilated, the boy swallowed a long string on which to thread a bougie, the string acting as a guide, and to quote from my report

"A short time after beginning the swallowing of the string he did not do well, although he continued to swallow the string until 12½ yards (11.43 meters) had been swallowed No food or liquids were retained, and the cough became very annoying In the meantime, the nurses' notes stated, 2 yards (1.83 meters) of string were recovered from the rectum This excess string was cut off with a scissors The patient was taken home and became progressively worse, coughing almost continuously and retaining no food and practically no fluids

"This continued for three days, when he was seen by Dr Daniel S Cuning of New York, who made a tentative diagnosis of abscess of the lung He was admitted to the Manhattan Eye, Ear and Throat Hospital on November 4, and further examination disclosed a piece of string in the larynx

"On November 5 an attempt to remove this string resulted in sudden asphyxia, and an emergency tracheotomy was performed by Dr Cuning The patient was immediately taken to the bronchoscopic room and 9½ yards (8.69 meters) of

string was removed from the right bronchus by Dr David Jones. The remainder, 44 inches (112 cm), was removed five days later by Dr Jones. The entire amount of string removed measured 10 yards and 26 inches (98 meters)."

It is obvious that a string should never be used as a guide in cases of tracheo-esophageal fistula because of the danger of looping itself around the tissue between the fistula, the trachea and the larynx.

This lad now has attained a growth of 48 inches (122 cm), weighs 47 pounds (21 Kg) and has no symptoms referable to his trachea.

The operation for the closure of the tracheoesophageal fistula was done on May 11, 1938.

DISCUSSION

DR LEE W DEAN, St Louis. How did you report last year that the fistula was closed?

DR CHARLES J IMPERATORI, New York. An incision was made through the trachea, and the fistula was exposed, that is, on the rear wall of the trachea, where the rings of the trachea do not come together. The wound was originally closed with linear sutures, with the hope that puckering would not result. Two months later it was found that the fistula was not completely closed. The wound was reopened. The patient was wearing a tracheotomy tube all this time, and instead of a linear suture a purse string suture was used. Originally silk had been used, but at the second operation all the silk sutures which were there and in place were removed and chromic catgut was used.

DR JOHN H FOSTER, Houston, Texas. How far down was the fistula?

DR CHARLES J IMPERATORI, New York. Opposite the fifth and sixth rings of the trachea.

DR JOHN H FOSTER, Houston, Texas. What was the original cause?

DR CHARLES J IMPERATORI, New York. Congenital fistula. He had had it all his life. In addition to the fistula he had a cardiospasm, which was treated by a physician previous to the time I saw him.

The credit in this case belongs to Dr McCullagh. He suggested that the boy had a fistula, and I took exception to that. I did not think it could be possible, but I was proved wrong.

Hygroma Cysticum Colli. Report of a Case. DR CHARLES J IMPERATORI, New York.

A swelling suddenly developed in the neck of a 7 month old baby and enlarged so rapidly within a few days that cyanosis developed. In order to breathe, the child automatically assumed the position of extreme extension. A roentgenogram showed a large mass located in the lower part of the neck extending from the clavicles to the jaw and laterally on either side of the sternocleidomastoid muscles. The trachea was displaced far to the right, so that it was considerably beyond the midline. There was also an atelectasis of the upper lobe of the left lung.

Aspiration demonstrated a bloody fluid that did not coagulate. Approximately 120 cc of fluid was removed, and 3 cc of a solution consisting of 0.75 per cent diathane hydrochloride (piperidinopropanedioldiphenylurethane hydrochloride), 5.5 per cent quinine hydrochloride and 3 per cent ethyl carbamate (urethane) was injected.

Roentgenograms taken after the injection showed that the trachea had returned to a more nearly midline position and the atelectasis had disappeared.

No recurrence has occurred after three months, and the child remains well. A subsequent report will be made on this patient relating to treatment and condition.

I saw a picture of this condition in Homans' Textbook of Surgery (ed 5, Springfield, Ill., Charles C Thomas, Publisher, 1940), which was published after I saw this child, and in a picture of his patient there was a mass which had localized directly over the clavicle. The mass in the child I saw was mostly on the right side.

coming toward the left but extending over the central part of the neck. The reason for using the fluid which I used was that on reading the transactions of the American Laryngological Society for 1935 (*The American Laryngologist* 57:39, 52, 1935), I found that a sclerosing solution had been used in the various hygromas that had been discussed over many years and particularly recently by Dr Carmody, who recommended a modified Carnoy's fluid, which consists of acetic acid, ferric chloride, chloroform and alcohol. This would seem to be a rather severe sclerosing fluid for use in a child, so I asked the urologists for something a little milder, and they recommended the solution they were using at the time in the treatment of hydrocele. Their object was to decrease the secreting epithelium, and this was practically the same effect I had under consideration. The diathane acts as an anesthetic, and the quinine acts as a mild sclerosing agent. The ethyl carbamate has a peculiar action on the endothelium—and this is rather theoretic—which permits the penetration of the quinine.

(Slides were shown)

Laryngeal Epilepsy, with Symptoms Conforming to the Pattern of Substantiated Cases Reported in the Literature. Report of a Case

DR JAMES A. BABBITT, Philadelphia

On Feb 1, 1940, A. H. was referred to me for treatment of an irritated, inflamed throat and chronic laryngitis following an attack of grip. The hoarseness varied in degree, but the throat was sore at all times, and there were an associated stuffiness of the eustachian tubes and some pain in the right ear. The patient reported that attacks like this had occurred before but never were so long in clearing up. He also had active acne rosacea. The examination showed that the patient had an irregular deviation of the septum, blocking both sides of the nose and making catheterization difficult. The faucial tonsils were rather small and were injected, with evident areas of cryptic secretion. On transillumination the frontal and maxillary antrums appeared clear. The tympanic membranes, though somewhat dulled, appeared normal.

The larynx was difficult to examine, as the right margin of the epiglottis had collapsed vertically, but the cords were clearly injected and thickened. In the course of the examination a pillar retractor was used to draw back the anterior pillar of the left tonsil and express cryptic exudate from the upper pole; semipurulent material appeared with this exudate. When this was done, the patient suddenly became cyanotic, with tremor of the body, twitching of the hands and a definite laryngeal spasm. When he resumed consciousness, there was an expectoration of much frothy mucus. Fortunately my assistant, Dr Silcox, observed this with me and can authenticate the details. This was a typical epileptiform spasm scarcely lasting even a minute, but its unusual character was striking. The history showed two definite attacks prior to this of the same character, one occurring six years before, after a vacation adventure in the mountains, when the party was gathered for simple refreshments, and a second one following a crabmeat dinner, three years ago, when the patient was taken from the table unconscious, and this state was reported to have lasted half an hour. The patient reported two or three minor occurrences of the same sort when he was alone. The patient was referred to Dr Tucker for examination and consultation. After the first examination Dr Tucker gave the following report:

"Mirror examination shows distinct thickening on both cords throughout the posterior third in front of the vocal processes. The thickening extends subglottic and seems to be in the nature of an infiltration, probably inflammatory. There is no indication for biopsy at this time."

As the patient had much postnasal mucus and threw back considerable fluid from the laryngeal area on examination, roentgen ray studies were made of the sinuses and for evidence of esophageal diverticulum. The following reports were made:

"Bryn Mawr Hospital, Feb 5, 1940 The examination of the sinuses shows extensive development of the sphenoid and ethmoid cells and slightly less extensive development of the frontal sinuses and antrums. Nowhere is there any density sufficient to suggest pathologic involvement. Individual ethmoid cells on both sides are large, and two aberrant cells extend upward into the frontal region and are separated from the frontal sinuses by distinct septums. The nasal septum is slightly deflected toward the left. There seems to be excellent aeration throughout both nares, with apparently no hypertrophy of the turbinates.

"Bryn Mawr Hospital, Feb 9, 1940 In both the upright and the semioblique prone position no obstruction to the flow of barium sulfate throughout the entire esophagus can be seen. Nowhere is there any sign of a diverticulum. However, on one of the roentgenograms rather large epiglottic valleculae are shown just anterior to and above the epiglottis, which is completely filled with barium and is somewhat larger than normal but should not, I believe, be considered a true diverticulum. There is otherwise no abnormality."

After considerable study for safeguarding the operation, there seemed to be two contributing factors: one was the marked nasal block of the cartilaginous septum, and the other was the exquisite tenderness and injection of the tonsils, particularly the left one. Manipulation of either area caused considerable laryngeal spasm. The tonsils were removed on February 29, and an abscess cavity in the posterior portion and involving part of the upper pole of the left tonsil, was found, perhaps 3 cm in diameter. The operation was done under local anesthesia and was handled well by the patient. Culture of material from the removed tonsils showed hemolytic streptococci. Convalescence from the operation was uneventful, and the patient has had no further attacks resembling epilepsy since the tonsils were removed, which indicates the importance of that focus.

A bibliography of some twenty references on this subject has been prepared and is at the service of any one who is interested in further investigation.

Myasthenia Laryngis. Observations on the Larynx as an Air Column Instrument. DR CHEVALIER L JACKSON, Philadelphia

This article will be published in full in a later issue of the ARCHIVES.

Benign and Malignant Tumors of the Jaw. DR FRANK R SPENCER, Boulder, Colo., DR CASPER F HEGNER (by invitation), Denver, and DR WILLIAM C BLACK (by invitation), Denver

This article appears in full in this issue of the ARCHIVES, page 200.

DISCUSSION

DR LE ROY SCHALL, Boston. When I first read the paper on "Benign and Malignant Tumors of the Jaw" I was struck by the high mortality rate.

At the Massachusetts General Hospital during the last ten years there have been 30 cases of malignant disease of the lower jaw, 29 patients being male and 1 female. The ages were from 49 to 77 years. The patients were treated as follows: 8 by surgical intervention, 16 by roentgen therapy, 1 by roentgen therapy and radium, 1 by surgical intervention and radium, 2 by surgical and roentgen therapy and 2 by radium alone. Of those who can be traced, 20 are dead and 1 is living (a patient treated surgically in 1926). Nine patients cannot be traced.

This group contained twice as many cases as Dr Spencer's, therefore, the results were just half as good as his. The high degree of malignancy and the high mortality of cancer of the lower jaw are emphasized. These results also emphasize the point brought out in Dr Spencer's paper: the necessity of early diagnosis.

DR THOMAS E CARMODY, Denver. Cases like this are observed in private practice. I have encountered about 120 of them in the last twenty-five years.

Many physicians are reporting on this condition in the lower jaw only. I have observed a number of nonmalignant conditions of the upper jaw. Of course, a few of these conditions are fibromas and conditions of that kind which are easily treated. Some of them remain cured for a long time.

(Dr Carmody then showed a large number of slides of various benign and malignant tumors of the jaw, including fibroma, fibroma durum, dentigerous cyst, follicular cyst, giant cell tumor, carcinoma, epithelioma and liposarcoma.)

DR FRANK R SPENCER, Boulder, Colo. One of the discussers reported a giant cell sarcoma in a young woman. I saw her about a year and a half after her operation, and she was all right. As might be expected, the condition was not malignant. There was no metastasis.

I have some hesitancy about reporting fatalities, but one really must expect them. The death rate from malignant disease is not as high as it was years ago.

The Larynx in the Tuberculous Patient DR ROBERT M LUKENS, Philadelphia

(Dr Lukens discussed the larynx as it is seen by routine examination of dispensary patients, in regard to symptoms, local changes and conditions influencing the health of the larynx in tuberculous patients. Suggestions were given as to the prophylaxis against laryngeal tuberculosis and the treatment of the larynx in tuberculous patients.)

DISCUSSION

DR BURT R SHURLY, Detroit. I have never personally observed a case of laryngeal tuberculosis in which the disease did not involve some other area, particularly the lungs. In sanatoriums from 8 to 15 per cent of all the patients show some involvement of the larynx. It seems to me that this percentage is diminishing under the more beneficial treatment which is now advocated and carried on under pneumothorax and general surgical treatment of the chest.

I have been particularly interested in what I think is the coming way of cutting down irritation in the larynx and diminishing cough and expectoration in cases in which there is cavity formation. The direct attack on the pulmonary cavities in tuberculosis opens up a field in advanced stages with interesting possibilities. Cavity suction drainage was first suggested by Dr Elser, of California, and the method was applied with a high degree of success by Monaldi, of the Forlini Institute of Florence, who succeeded in closing 42 per cent of the cavities operated on.

Any procedure less drastic and mutilating than thoracoplasty which offers possibilities of as good or better results should certainly be thoroughly investigated. If thoracoplasty and pneumothorax had given ideal results, such exploration in new fields would be unnecessary, but when they are applied in the advanced stages of the disease—and, of course, thoracoplasty is reserved only for such—they often fail. Pneumothorax also in advanced conditions, even with the help of Jacobsen's pneumolysis, often fails. Both pneumothorax and thoracoplasty fail more appreciably as the contralateral lung is invaded. It is almost always difficult to persuade patients to submit to thoracoplasty. There is no such difficulty in advising cavity suction drainage, which is usually a simple operation requiring only local anesthesia. Localizing and entering small cavities present some difficulty, which will be eliminated to a large extent by improving methods of localizing cavities which are caused by continuous pressure in a weakened area, such as softening tuberculous areas afford. If the influence of positive pressure is removed the cavity will tend to close. Suction drainage accomplishes this. The normal tissue is capable of great hypertrophy and rapidly reoccupies the space formerly occupied by the cavity.

In many cases coughing and expectoration are controlled, and this not only is of great relief to the patient but lessens the influence of the pressure, which is greatly increased by coughing.

It is much better to have the cavity detritus in a bottle than passing the trachea, larynx and mouth, thus lessening the chance of infection of normal tissue or the opposite lung. The operation is so simple as far as shock is concerned that it has a tremendous advantage over the more radical treatment.

My associate, Dr Bullock, opened up an entirely new field in his suggestion of treating the walls by the application of digestins, such as enzymol and papain. It is well known that cavity walls do not have a healable surface. They are backed by scar tissue and present a dirty gray mass of caseous tissue loaded with bacilli. Dr Bullock's idea is to create a healable surface with simple digestants, which, if they do not give the desired result, should be superseded by others. Many of these suggest themselves. Cauterization or application of solution of iodine may be used.

In 1 case, of which I have personal knowledge, the large cavity occupying most of the upper lobe of the right lung was operated on on Dec 12 1939. Weekly roentgenograms ever since have shown a continuous reduction in the size of the cavity, until now it is barely discernible. It was filled with enzymol each night for ten hours, and then suction was applied for the remainder of the twenty-four hours. Coughing and expectoration stopped within a month, and the material draining from the cavity became free from tubercle bacilli in six weeks and has remained sterile to date.

In the institutions under my direction, 17 patients have so far been operated on, and in nearly all the results are encouraging. It should be remembered that this procedure is applicable in cases in which the condition is bilateral and in which both pneumothorax and thoracoplasty are considered not possible, it is my conviction that it is worthy of extended trial. I feel that this new method in cases of laryngeal tuberculosis will decidedly improve the condition of the larynx. It will do away with the tubercle bacilli in many cases and will do away with radical surgical procedures required in later stages of the disease.

DR GEORGE B WOOD, Philadelphia. Dr Lukens feels about tuberculosis as I do about nasal sinus disease. He is conservative in his methods of treatment of laryngeal tuberculosis, while I am very conservative in the treatment of the sinuses. Except in the far advanced cases in which every form of therapy is hopeless, I do not know that there is any type of lesion in which, to my mind, the use of the electric cautery is contraindicated.

I think there has been a great decrease in the number of cases of laryngeal tuberculosis in recent years which is directly traceable to the use of the collapse therapy, because in the large majority of the cases laryngeal involvement is due to contact infection from the sputum coughed up by the patients.

However, a series of articles has recently been published (Wessely, E. *Zentralbl f d ges Tuberk-Forsch* 50 393 [June 24] 1939, Spira, J. *Monatschr f Ohrenh* 72 700, 1938, Knapp, E. *Hals-, Nasen- u Ohrenarz* (Teil 1) 29 303 [Sept] 1938, Eschweiler, H. *Ztschr f Hals-, Nasen- u Ohrenh* 43 163 1938, Blomroos, T. *Acta oto-laryng*, 1938, supp 28, pp 1-159, Randerath, E. *Ergebn d ges Tuberk-Forsch* 9 145, 1939) which, to my mind, definitely proves that more of these cases are hematogenous in origin than I like to believe. It has been shown by histologic examinations where there is no visible tuberculosis of the larynx, even when removed at autopsy, that there may be tubercles in the ossified structure of the laryngeal cartilages. These tubercles do not occur in the cartilage, but where the cartilage has become ossified tubercles have been found in the medullary substance of the bone. Without any other evidence of tuberculosis, they could not come from the surface, so it must be that a certain number of patients have hematogenous involvement of the larynx. The difficulty, of course, in treating laryngeal tuberculosis is in making the diagnosis early, and the part that is most difficult to see by the indirect method, or even by the direct method, is early involvement of the ventricle. This, however, can frequently be visualized by roentgenograms, and I think roentgenograms of the larynx in doubtful cases are important.

I should like Dr Lukens to mention his technic in the use of chaulmoogra oil, I have never become enthusiastic about this method, always realizing, though, that Dr Lukens is getting results where I fail to get them. I should like to know how frequently he uses the chaulmoogra oil in the larynx. Of course, publications as to

the action of chaulmoogra oil show that it does have an effect in producing active congestion of the larynx. It is the increase in blood supply to the larynx and to the local lesion which brings about spontaneous healing. The object of cauterization is not the destruction of the mass itself, it is the revascularization by the formation of granulation tissue necessary to throw off the eschar which revitalizes that vascular area.

DR FRANK R. SPENCER, Boulder, Colo. I believe that with the improved methods of surgery more and more tuberculous patients are suitable subjects for surgical treatment, but there is some danger in making such a statement, for sometimes younger otolaryngologists, overeager to use surgical therapy, hasten a fatality. Certainly patients with advanced tuberculosis are not and never have been good risks for any type of surgical procedure.

I said something this morning about lactic and trichloroacetic acids, these should be used in dilute strength if they are used at all. Personally, I would rather use cautery. I do not believe surgical diathermy is as useful as cautery for laryngeal tuberculosis.

I was glad to hear Dr. Wood say that collapse therapy has done a great deal to prevent laryngeal tuberculosis. I certainly am seeing much less of it than I did, for two reasons: first, because collapse therapy prevents it and, secondly, because most states now have sanatoriums for tuberculous patients and they are not sent to the West.

Whispering is of tremendous advantage.

During the past few years two British laryngologists (Grain, R. *Tubercle* 17 261, 1936, Cotton-Cornwall, V. *Lancet* 2 1109 [Nov] 1938) have advocated ionization to relieve pain in the advanced stages instead of injecting alcohol into the superior laryngeal nerve. There is some advantage in ionization. The method is easy to use, it is easy to continue the anesthesia, and in late stages it may be better than the injection of alcohol into the superior laryngeal nerve.

Tracheotomy, as Dr. Lukens has said, may be useful in emergencies. I believe in every instance in which I have had to do a tracheotomy it has been for late laryngeal tuberculosis and consequently I have obtained no brilliant results.

DR THOMAS E. CARMODY, Denver. How about limiting the motion of the arms, as Negus has suggested, in the quieting of the patient? How about the restricting the use of the voice? Negus stated that the bringing of the cords together causes the congestion of the cords.

DR ROBERT M. LUKENS, Philadelphia. I have read about it but I have no experience with it.

This paper was written entirely on ambulatory patients and not on hospital patients in the advanced stages. The treatment is one which is primarily preventive.

In both the Jefferson Medical College Hospital and the Henry Phipps Institute, pneumothorax, pneumolysis and thoracoplasty are used wherever indicated. The tuberculous patients are seen in the dispensary. I examine most of the patients, particularly in Phipps Institute. At present I should say that less than 10 per cent are tuberculous. I mean that the incidence of tuberculosis is much lower than it used to be. There has been a great decrease, and I think that is mainly due to early examination and also to the methods used in the chest department.

As far as cautery is concerned, I have had little occasion to use it on this class of patients. I do use the cautery and also use it for ulceration and infiltration when the other milder methods fail. I have found that in early cases the larynx has a tendency to take care of itself pretty well, provided everything else is equal.

As far as chaulmoogra oil is concerned, I first used it in a case a good many years ago. It was a case in which there were many vegetations in the posterior wall of the larynx. The patient had extensive ulcerations of the ventricular band in the posterior half of the larynx which was involved and advanced tuberculosis of the lung. I administered lactic acid and formaldehyde and treated him for a year and then used the cautery on the posterior wall, I forget whether it was three or four times. The vegetations came back and the ulcerations did not

clear up Then I started treatment with chaulmoogra oil, entirely in the larynx, although it was being used for other types of tuberculosis I knew at that time The larynx cleared up in about six to eight months Since then I have been using it right along The chaulmoogra oil does cause some passive or active congestion of the mucosa, as near as I can see clinically, but some of the patients require cautery, so I cauterize them I felt on one occasion that I had cauterized too extensively and had to go back to administration of the oil to relieve the patient from dysphagia

The Use of Laminagrams in Laryngology DR LEE W DEAN, St Louis, DR ALFRED J CONE (by invitation), St Louis, DR WILLIAM BURTON (by invitation), St Louis, and DR SHERWOOD MOORE (by invitation), St Louis

In common with all roentgenography, that known as body section roentgenography is of the greatest use where there is the natural contrast in density, which obtains more fully in the case of the respiratory tract than elsewhere The laminagraph early demonstrated the fact that lesions in the pulmonary area, completely undiscoverable by any other method of examination, were clearly demonstrated and accurately located Somewhat later it was found revolutionary in the examination of the paranasal sinuses, particularly in the posterior ethmoid and sphenoid cells It has contributed heavily to a more complete understanding of lesions involving the larynx and holds great promise for the study of subglottic involvement Farther down the tracheobronchial tree not only is information obtainable in the larger divisions but occasionally information is discovered in bronchial branches the size of which is of the order of 3 to 4 mm

DR LEE W DEAN, St Louis Dr Moore devised the instrument, the laminagraph, and developed the technic for its use

Dr Cone did the research work on the nasal accessory sinuses and followed it up with clinical work All I had to do with the investigation was to select certain cases in the clinic for study and pass judgment on the results

The use of laminagrams has helped in the study of certain difficult cases of disease of the nasal sinuses

(Dr Dean showed slides and laminagrams of 3 patients)

The first patient was an undergraduate nurse, about 23 years old, with retrobulbar neuritis of the left eye Her vision was 1/60 in the left eye The right eye was normal She had been in the hospital for five days being studied by members of the departments of ophthalmology, medicine and otolaryngology Other members of the staff and I had studied the upper part of the posterior sinuses, using roentgenograms and of course making a careful clinical examination It was my opinion that the upper posterior part of the nose was normal This opinion was confirmed by other members of the staff No evidence of disease of the sphenoid or ethmoid sinuses was found None of the common or unusual causes of retrobulbar neuritis were found The question of exploratory operation on the upper posterior sinuses was discussed, but I was not in favor of it, because there was no indication of sinus disease Laminagrams were taken Dr Moore read them and said that there was some abnormal condition in the left ethmoid and sphenoid sinuses Dr Cone agreed, but he thought the blurring on the left side indicated infection of the sinuses The laminagrams caused a change in opinions, and operation on the left ethmoid and sphenoid sinuses was advised The tissue removed at operation showed a heavy round cell infiltration

After the operation there was a rapid return of vision to normal

The second patient, about 57 years of age, had bilateral retrobulbar neuritis I am inclined to think that the bilateral type often is not due to sinus disease That was one reason why I procrastinated in advising operation on the sinuses in this patient The patient had been studied by a competent ophthalmologist and by an otolaryngologist for nine months previously

There was a moderate amount of sinusitis, but in my judgment it was not definite enough to indicate operation on the sinuses at that time. The patient was observed and turned over to the various departments for study. After four months of observation his vision was continuing to get worse. During this time he received the usual treatment, shock therapy and vitamin B₁ by injection. At the end of four months laminagrams were taken and at a depth of 6 cm showed a marginal thickening of the lining of the ethmoid cells in each side. One side was operated on and later the other. On each side at a depth of 6 cm a tumor-like thickening of the lining with the ethmoid cells was found and removed. These masses consisted of infected tissue. The operation was followed by marked improvement in the better eye and less improvement in the poor eye. A year after the operation, he had practically normal vision in the better eye.

In my judgment it was only after the laminagrams were taken that there was sufficient pathologic change in the upper part of the posterior sinuses to justify the operation. When he was operated on, much to my surprise, the surgeon who had been told by Dr. Moore just what cells were diseased was able to attack only these cells and neighboring cells without eviscerating the whole of the ethmoid labyrinth. At operation the findings which Dr. Moore had predicted were confirmed. By taking laminagrams of various depths, one is able to predict just what ethmoid cells are involved, and this permits the surgeon to attack only these cells.

The third patient is a girl, aged 7 years, who came into the Children's Hospital with an acute hemorrhagic nasal infection, which had developed during a severe head cold. There was a purulent discharge from each side of the nose which contained pneumococcus type XII. The tonsils appeared normal.

Laminagrams were made of the nasal sinuses. Much to our surprise, there was as much, if not more, infection in the upper posterior sinuses than in the maxillary sinuses. My associates and I have paid so much attention to infections of the maxillary sinus in young children that it has given us a new thought in using the laminagrams. Treatment of the sinuses was resorted to, this plus chemotherapy, which was discontinued because of the severe reaction of nausea and vomiting, produced a rapid improvement.

DR. SHERWOOD MOORE (by invitation), St. Louis. It is generally conceded by any one who has used this method that in chest work it is invaluable. Its application to treatment of the paranasal sinuses has also been invaluable.

(Dr. Moore then showed a number of slides illustrating the application of laminagraphy to the diagnosis of lesions in the chest.)

(Dr. Cone showed a number of slides illustrating just how laminagrams of the sinuses at various depths are made and comparing the laminagrams of various patients with roentgenograms taken in the conventional manner. His slides indicated how this method could be utilized to study the varying anatomy of the ethmoid and other sinuses.)

DISCUSSION

DR. FREDERICK M. LAW, New York. If I were to criticize this work at all, I should say the laminagrams lack the detail to which I am accustomed in the conventional roentgenogram, but this method is in exactly the same state that roentgenograms of the sinus were in the early days, and see how they have improved since then. What this method is going to produce in a few years will probably be marvelous.

I am sure that in combination with good stereoscopic and standard roentgenograms laminagrams will show and locate conditions which are only assumed in the conventional type of film. I am overwhelmed with enthusiasm.

DR. CHEVALIER L. JACKSON, Philadelphia. My associates and I are finding the use of body section roentgenography of great value in treatment of bronchopulmonary disease and disease of the larynx. I should like to mention 2 cases of foreign body in which this method proved of great help to us recently.

A patient had a piece of glass in the esophagus which showed plainly in the lateral roentgenogram, but the shape could not be made out in the anteroposterior roentgenogram. As the object was sharply pointed, it was desirable to know what the shape was and which way the points were projecting, if possible. With the use of laminagraphy it showed up beautifully as a long object with two points, one much higher than the other, and these points were both perforating to some extent on both sides.

In the other case a fragment of a tooth had lodged in the bronchus of a child. The fragment was well down in the branch of the lower bronchus, and it was difficult to visualize by fluoroscopy because of the pulsation of the heart on the left side. It was not removed with the bronchoscope at the first biplane fluoroscope visualization, but laminagraph studies showed that it was definitely localized just posterior to the stem bronchus rather than just anterior to it, as it was thought from the ordinary roentgenograms. The film at 5 cm showed the tooth and began to show the bronchus. At 6 cm it showed the bronchial lumen mainly, and in the one at 7 cm neither the bronchus nor the tooth showed up. It was concluded, therefore, that the fragment of tooth was just posterior to the stem of the bronchus.

DR SAMUEL SALINGER, Chicago. In the last two weeks I have observed 2 cases of retrobulbar neuritis in which the conventional roentgenograms failed to show anything definite but in which the laminagrams definitely demonstrated shadows in the posterior ethmoid cells.

It may become a general belief, as in France, that in practically all cases of optic neuritis the condition is due to pathologic changes in the posterior cells, which should be operated on.

One possible field for the use of this procedure which has not been explored is body sectioning at the level of the petrous bone. I failed to see any mention of it in the literature and do not see why it is not possible to take pictures at such a level as to show the petrous bone at various points and possibly demonstrate pathologic changes which up to now have not been noticed.

DR SHERWOOD MOORE (by invitation), St. Louis. The method has revealed the course of the auditory canal throughout its entire extent, and we have been able to show enlargements of the internal auditory meatuses in tumors of the eighth nerve.

The American Laryngological Association The American Board of Otolaryngology An Integration Survey DR WILLIAM P. WHERRY, Omaha

(Briefly this paper dealt with administrative proposals bearing on the American Laryngological Association, the American Board of Otolaryngology. The theme concerned graduate medical education.)

DISCUSSION

DR HARRIS P. MOSHER, Boston. This paper is carefully and at times subtly worded. It is a challenge. It points out opportunities and duties. Some years ago I was on somewhat the same tack. I had little success.

Dr. Wherry constantly referred to graduate education. As a member of the Advisory Board of the Specialties I had a chance this year to sit in at some of the meetings in Chicago of the societies of men who earn their living by teaching. There is a real revolution going on in the methods of teaching. There is a beehive of activity at present over this subject. Some of it I cannot understand.

There are one or two things of which I should like an explanation. What was the battle of Milwaukee? What is a "mechanized mind"? What are "faculty contacts," and are they really worth anything?

DR RALPH A FENTON, Portland, Ore The Council on Medical Education of the American Medical Association has been referred to I want to say, speaking as a trustee of the American Medical Association, that the Council has welcomed of recent years the cooperation of the various boards, and it is due to that cooperation that the boards have received the recognition of the American Medical Association That recognition, however, has been under attack

DR BURT R SHURLY, Detroit The problems that have been met and considered during the past fifteen years are revolutionary and evolutionary in the light of higher standards of education

Today practically complete obliteration of graduate education abroad confronts physicians America has a new problem to meet Many physicians have derived much in the way of inspiration and education from the various centers of Europe It therefore becomes a duty to concentrate in the American institutions on newer and better graduate education The solution of this entire subject is necessarily dependent on cooperation of all the various societies There has been a battle to have the specialties recognized as they should be I feel, however, that conditions are on the up-grade and that wonderful improvement in graduate education is at hand The difficulties are great in properly preparing graduates in otolaryngology

More than a hundred applications have been received for the two places in the Shurly Hospital, which I have conducted these many years I simply mention this to show that the demands of the person who wishes to better himself are great and the opportunities are insufficient It, therefore, behooves members of this, the senior society, to get behind this improvement in graduate education I think the idea of a committee of interest is good I was on such a committee more than twenty-five years ago in the society in which the ideas were first formulated The idea of this advisory council is certainly a step upward and onward in making all graduate education an equal, improving system of education I feel that the great universities of this country should be behind graduate education in a better and a finer way There are comparatively few medical centers Under suggestion and under plans of improvement, I feel that the work can be accomplished in America without the necessity of looking to foreign centers The advisory council should be a cooperating body to lay out the program in combination and in cooperation with all the various activities and all interests, so that cooperative work can accomplish the things which are now deficient in certain parts of this country

Examination of 2,500 or more men who desire further education shows that many of them are deficient in their knowledge of anatomy and pathology This condition is being greatly improved, but the problem of graduate education must be brought into each center of medicine in this country

DR CHARLES J IMPERATORI, New York I probably represent the periphery, the average person in the American Laryngological Association I do not represent nor do I know the inner workings of the various boards I do know that there are certain universities and there are certain men who desire to allocate to themselves the right to do as they please regarding graduate medical education

I think that Dr Wherry has developed the idea absolutely correctly and definitely in that the teachers who are teaching in the various graduate schools are not competent and it is for us, as members of the senior society, to tell them they do not have proper and adequate means to train students who come to them It is difficult and embarrassing to get up and make these statements, but nevertheless I have felt that many teachers were not up to standard in teaching these students They were taking the students' money, but they were not giving them the goods

I am in favor of, and not because I am on the outside, the work done by such physicians as Dr Mosher, Dr Wherry and Dr Shurly over the past twenty-five years I know they have given a great deal of time I know nothing about these various battles except what I have heard, as it were, on the periphery, but I certainly am in favor of raising the standards of graduate education

When a surgeon's child has otitis media, the surgeon certainly does not go to another surgeon, he immediately goes to the otolaryngologist. Therefore, I feel that this specialty should be a major specialty and not a secondary one, a mere subsidiary to the department of surgery.

DR WILLIAM P. WHERRY, Omaha. Within the next seven years the whole scheme of medical education will be revamped. This may seem to be a startling statement. The specialties will be allocated to the graduate field of medicine, with certain fundamentals in the undergraduate.

The intern year, which heretofore has been a haphazard affair in a large number of instances, will become an integrating unit from which and in which the medical student will orient himself as to where he will drift.

My colleagues and I spent two years in a study of anatomy, certain of the younger members in the more recent years have spent a semester. We dissected a cadaver, we learned every muscle, its attachment, its blood supply and its nerve supply. Within the next seven years that will be a part of graduate medicine. The undergraduate will be taught anatomy, in a large measure, in the library.

Administrative leaders say that it is absurd that a man going into the field of internal medicine should spend that amount of time at dissecting. They recognize, however, that a surgeon needs such work.

Now the time has come when as a part of this reorganization, this revamping—it does seem, as one looks at the world in its entirety, that there is something new and coming and it seems to be distributing its influence in the scientific world as well as in the economic world—it would seem fitting that those who are particularly trained, who are teachers in special fields, should be not only interested but actively interested in the plans.

The battle of Milwaukee refers to the time when—in Chicago first and then at Milwaukee—for a week or ten days the fate of the whole board probably hung by a thread, but good medicine prevailed and the boards won out. Full credit should be given to Dr. Ralph Fenton and to Dr. Samuel Kopetzky, who were in the House of Delegates of the American Medical Association.

In answer to the question on "mechanized minds," there is a lot of difference between a parrot—a person who says what he has read in a book or tells what some one has told him but does not know reasons or explanations—and a person with a reasoning mind.

I think the phrase "faculty contacts" expresses itself. There has come into the language of those who are interested in medical education the expression "faculty contacts." The expression "faculty teaching" does not carry the meaning. Contacts with members of the faculty embrace all contacts. I do not believe any one present can define "culture," but it is demonstrable. If a student embraces in himself some member of the faculty as his hero, and if that man, that faculty contact, can instill in the student that something called "culture"—not in the classroom or necessarily in the clinic or elsewhere—the faculty contact is all embrative.

The Nasopharynx DR S. J. CROWE, Baltimore

This article will be published in full in a later issue of the ARCHIVES.

DISCUSSION

DR THOMAS E. CARMODY, Denver. I think this paper is timely and interesting, because I feel that many otolaryngologists do not examine nasopharynges as well as they should. It is difficult to examine them in children, and I find that they are frequently overlooked even in adults.

Adenoid tissue is found in adults almost as much as in children, not soft but firm adenoid tissue. I should like to ask Dr. Crowe whether he treats the lateral folds behind the posterior pillar as well. I think Dr. Crowe's treatment with radium is satisfactory. I have not used it, I have only the radium salt and not

the radium emanation, and this treatment with the salt takes too long. He suggested forty minutes for the radium salt, but that is too long for a child.

I have tried radiation with roentgen ray therapy, but it has not been satisfactory. I should like to know how Dr. Crowe examined the nasopharynx in these children. In some children an anesthetic is needed if they are going to be examined thoroughly with the finer nasopharyngoscope and the oral speculum.

DR SAMUEL J. CROWE, Baltimore. The question of examination of the nasopharynx in children with the nasopharyngoscope is largely one of mass psychology. Since October the school nurses and the nurses of the department of health have brought into the hospital each morning and each afternoon groups of from 18 to 25 children, all between 8 and 14 years of age. Of 1,400 children, 1,365 were perfectly satisfactory on examination, just as satisfactory as any adult, but the examinations were done where the rest of the children could see the one undergoing the test. If one that does not seem to be too highstrung and nervous is chosen for the first examination and then the rest of the children are allowed to observe the examination, it is perfectly simple and easy.

As for the treatment of the lateral pharyngeal walls, the posterior pharyngeal walls and the tonsils at the base of the tongue with radium, I have never undertaken that because of the great danger to the operator. The only protection the operator could have against the use of radium is distance. One is not protected by wearing gloves, as in a fluoroscopic examination. I place the applicator in the nasopharynx and then immediately get away. If one wishes to treat effectively the pharynx or the tonsils with radium, it would have to be held in place, or the region must necessarily be treated with roentgen rays.

DR HAROLD I. LILLIE, Rochester, Minn. This problem of hypertrophy of lymphoid tissue in the nasopharynx has interested me for many years, and I have made some suggestions as to methods of treatment before this society.

My colleagues and I have made observations similar to those reported by Dr. Crowe. We observed that the application of radon to the region of the torus of the eustachian tubes and the fossa of Rosenmüller was effective in controlling that region. The fact, however, that many patients are successfully operated on for removal of adenoids and tonsils and apparently do not have recurrences of lymphoid tissue in the nasopharynx suggests to me that in those persons who do have recurrences there is something fundamentally lacking in their makeup or that in them the tonsillar tissue must serve some function.

I am not ready to deny that the lymphoid tissue included in the pharyngeal tonsils in children does not have some function. We have observed a group. Of course, I cannot quote any such numbers as Dr. Crowe has on account of the nature of our situation, but I have made observations for over fifteen years on some children in the city, and I have found that many of them lack certain things in their diet. I have seen several instances in which when a patient was required to eat the fat of the meat along with the lean his nasopharynx definitely changed in two or three months.

The use of iodine in some form has been suggested. We have found that hydriodic acid in certain children is not as effective as it should be because of the lack of iodine content, but sodium iodide can be given to these patients rather successfully and with gratifying results.

So far as the hypertrophy of the lateral pharyngeal band is concerned, it may be compensatory, as I suggested. In this group of patients we have found electrocoagulation to be the most successful method of treatment if other methods fail.

DR SAMUEL J. CROWE, Baltimore. Baltimore is the ideal place right now for the investigation of the causes of such conditions as lymphoid hyperplasia and impaired hearing in school children, because of the location of the School of Public Health and Hygiene in Baltimore. In order to have a practical working ground for the students of that school, the Rockefeller Foundation has financed for many years what is known as the Eastern Health District, which is a district of respectable wage-earning people who work in the various steel and oil industries.

scattered along the waterfront. For fifteen years or more the families in this group were found to be rather stable, that is, they do not move frequently, and they have been surveyed from every point of view. They are accustomed to it. They like to be surveyed.

This year the investigation only supplements that which has been carried on since 1924 as regards the causes of deafness.

Up to the present year my fellow workers and I have attempted to study deafness by correlating the functional tests of hearing with the histologic appearance of the temporal bone studied in serial section after death. This method has a great many shortcomings. It tells little about how the deafness began, how it progressed or how rapidly it progressed and leaves no definite ideas as to what to do for it. The present study on children was undertaken to supplement this program.

Here are 1,300 to 1,400 living, growing temporal bones which can be followed from year to year. The hearing tests are all made in sound-proof rooms with the audiometer, which tests from 32 up to 16,384 frequencies, and it is perfectly certain in the early stage of impaired hearing of all types, with the possible exception of otosclerosis, that the impairment begins in the high frequencies, first, 16,000 and then 13,000, 10,000 and 8,000. It has its beginning there and progresses. That is what is meant by progressive deafness. It progresses toward the speech range, sometimes rapidly and sometimes slowly.

It is planned and hoped to continue this observation next year in two ways, first, to continue observations on the large group. Thirteen hundred to 1,400 children were examined this year, of whom only 62 per cent were found to have normal hearing and 38 per cent impaired hearing. Those with the most marked impairment—and they amounted to about 250—were treated with radium alone in order to avoid complications. About 300 or 325 with slighter impairment of hearing were set aside as controls and had no treatment of any kind. This study will be continued next year and, we hope, the next year and the next.

In addition to that, we should like to examine another 1,000 children in the same way, to pick out those who have the most impairment of hearing and most marked lymphoid hyperplasia and, in addition to giving the therapy that has been used before, that is, removal of the tonsils and adenoids and radium treatments, to administer vitamins, particularly vitamin B. We have some reason to suppose that vitamin B deficiency is connected with degeneration of nerves in other parts of the body. If no other elements of food are given except that and if the percentage of children in whom hearing improves is increased, the cause of improvement will be definite.

DR GEORGE B. WOOD, Philadelphia. I wish to say just a word about the importance of food in hypertrophy of lymphoid tissue in the pharynx. Some experimental work has been done under the supervision of Professor Clark, Professor of Anatomy of the University of Pennsylvania (Sattles, E. S. *Anat Rec* **20** 61, 1920; Lefholz, R. *Am J Anat* **32** 1 [July] 1923). He fed a series of young cats various types of food for a varying length of time and then studied the lymphoid tissue not only in the region of the tonsil but also in the gastrointestinal tract. I have seen his photomicrographs and noted that the increase in lymphoid tissue from rich foods, especially food containing a great deal of fat, is remarkable. The Peyer's patches were three times as thick in cats fed on rich food and a high degree of fats.

DR JOHN L. MYERS, Kansas City, Mo. My interest in this subject was first stimulated when I found that the roentgen rays act first on the lymph cell and that after an animal has been exposed to roentgen rays, within fifteen minutes the lymph cells show a reaction by a decrease in their number. I began wondering if one could not shrink the tissues in the throat by using roentgen ray therapy, and I have used it on a number of cases. I have had a number of patients who have complained of postnasal dripping due to the lymphoid tissue, and I have had some success and some failures with irradiation.

I should like to ask Dr Crowe what vitamin B product he suggests for use. I think there are about ten or fifteen kinds. There are many fractions: thiamine chloride, riboflavin and various others. I now use the vitamin B complex.

DR SAMUEL J CROWE, Baltimore. As yet I have had no experience with vitamin B. I only mentioned it as a point of interest in the hope that if this country is spared in this war and if world conditions warrant, an investigation of that kind might be undertaken.

DR SAMUEL SALINGER, Chicago. According to Dr Crowe, the ideal method of treatment is to apply a maximum amount of radon so that the period of application will be brief. As is well known, machines for the extraction of radium are rare throughout the country. There are few places that have a sufficient amount of radium to be able to give a thousand millicuries. It seems to me that for a thousand millicuries of radon one would require something like 7 or 8 Gm of radium, which is a good deal.

I have often wanted to use roentgen ray therapy, but I was more or less in fear of causing damage to the pituitary body by scattering radiation and of the possible arrest of development of the salivary glands. For that reason I have never advocated the method, although I think it might have some merit. It seems to me there is some room for investigation with regard to the use of roentgen rays, which are available everywhere and could be applied so that this method could be more universally employed.

DR JAMES A BABBITT, Philadelphia. Dr Crowe, will you answer that?

DR SAMUEL J CROWE, Baltimore. I tried to outline in this talk the possible objections to roentgen rays, that is, the accuracy of delivering the rays at the point where they are most needed, particularly in children—and it is children that I am talking about and not adults—also the possible influence of such an excessive dosage, half of which is absorbed by the tissues in the neck, on the centers of ossification of a growing child. Third, but not least important, is the fact that the otolaryngologist must refer his patient to a roentgen ray technician or radiologist who knows little about the local conditions and the varying anatomic structures and often turns treatment over to a technician. It is much better, if radiation therapy is going to be introduced into otolaryngology, that the otolaryngologist himself carry out the treatment.

What has been said about radon is true. Physicians in Baltimore are happily located, as far as the supply of radon is concerned, because Dr Howard A Kelly, a gynecologist, has had a private hospital for many years and has collected a large supply of radium. He and Dr Burnham, his associate, have always been interested in supplying radon for experimental purposes of all kinds, so that an abundant supply of it is available at a nominal cost, just the cost of the technician. In New York, Philadelphia, Boston, Detroit and other cities radon from a commercial firm costs \$2 per millicurie, so that even a 500 millicurie applicator, and I use one much stronger than that, would cost \$1,000. The price makes it impossible for this method of treatment to become universal, unless the departments of health, the state, the city or the federal government supply the radon.

DR HORACE NEWHART, Minneapolis. The one point I should like to make is that the fame of this work has gone out among the medical profession and also among the laity, and I can see great danger of mishandling on the one hand and of quackery on the other. I think Dr Crowe expressed this fear to me over a year ago. I have already seen the effect of it among friends who inquired about it. I think conservatism and care should be exercised. There is the question of making some experiments or other efforts to determine the incidence of high frequency loss among the younger patients.

What do you consider the criterion for normal and abnormal hearing deficiency for the higher frequencies, and how high do you go? Do you consider it important to test up to 11,000 or beyond, or do you get enough information from the frequencies from 4,000 to 10,000 to serve as a reliable criterion?

DR SAMUEL J CROWE, Baltimore In the first place, I am perfectly sure that not more than 65 per cent of the ordinary healthy, apparently normally hearing children in school actually have normal hearing

All of these 1,400 children had already been examined by the city authorities with the phonographic audiometer and the 1A audiometer tests up to 8,000 double vibrations, so the children we examined were those supposed to have normal hearing both by the teachers and by their families As a matter of fact, there were about 35 or 38 per cent of those that had abnormal hearing, as evidenced by impaired hearing for frequencies of 8,000, 10,000, 13,000 and 16,000 The loss in hearing begins with the 16,000, 13,000 and 10,000 frequencies, and as it gets a little more advanced, it affects the 8,000 and 4,000 frequencies, and when it affects the 4,000 it is getting dangerously close to the speech range That is exactly the type of hearing defect that most people have in old age, that is, good hearing for low tones and impaired hearing for high tones It is also known that an elderly person with that type of impaired hearing has no difficulty whatsoever if one speaks to him in quiet surroundings, but at a dinner table or in a room where there are several people talking and a background of noise he is terribly confused and misses many things That is exactly what happens to children in school

The children were selected by testing the hearing of whole groups of children from a school In an investigation of their school work with their teachers it was found that they are the ones in the class that have failed or are regarded as mischievous, inattentive or not very bright, while, as a matter of fact, they miss a good many things because of the background of noise in a large classroom

DR BURT SHURLY, Detroit In regard to hearing tests of school children in Detroit, where about 100,000 children are tested, observations indicate that 48 to 52 per cent show loss of hearing

I feel that I should arise in defense of the 30 year old Shurly soup which has been used over the country and which really was the key to this situation, in a way, before the word "vitamin" was ever heard of By extensive investigations after the removal of tonsils and adenoids in children in many thousands of cases it was found that while a vast majority were greatly benefited, there were always some with malnutrition or with lymphoid tissue that grew rapidly again, and that underneath it all was a dietetic problem of mineral salts and vegetables The soup consists of two carrots, two beets, a bunch of celery, two potatoes and two tomatoes and together with cod liver oil furnishes a balanced diet

DR JAMES A BABBITT, Philadelphia I should like to ask Dr Crowe what local anesthetic he uses for children and how he uses it

DR SAMUEL J CROWE, Baltimore I use a 20 per cent solution of cocaine hydrochloride, I moisten a cotton-tipped applicator with this solution, wringing out the excess, and apply it to the floor of the nose This solution has not produced any reaction in the children that have been examined this year, and they were examined at the rate of 30 to 50 a day by a group of persons who do nothing else If no excess cocaine is allowed to run down the throat and be absorbed, the solution has no toxic effect whatsoever and is much better than a 5 or 10 per cent solution, because it takes a shorter time There are no sprays of any kind for this purpose

Laryngologic Aspects of Sporadic Infectious Mononucleosis DR WILLIAM E GROVE, Milwaukee

This article will be published in full in a later issue of the ARCHIVES

DISCUSSION

DR JOHN J SHEA, Memphis, Tenn It is of more than academic interest to be able to make a diagnosis of acute infectious mononucleosis under certain circumstances Enlargement of the cervical glands in young girls is sometimes feared as the beginning of a more serious condition, such as early Hodgkin's disease or an acute lymphocytic type of leukemia

The lower part of an ordinary hemogram in these patients is of interest. The granulocytic type of white blood cell, of course, includes basophils, eosinophils and neutrophils, but the lymphocytes and the so-called monocytes are the cells that increase in this condition.

For these young women, usually of the better class of patients, in whom glands are beginning to enlarge, a condition which has lasted past a febrile stage, and who have an increased white blood cell count, 12,000 to 14,000 per cubic millimeter, if one can make the diagnosis of acute infectious mononucleosis all worries will be relieved. This condition is a self-limiting disease, and the patient will get well if simply treated symptomatically.

A girl, 12 years of age, was of a family which had 2 or 3 friends in whom Hodgkin's disease had developed. The persistence of the enlargement in the cervical glands caused alarm. Her first blood picture showed 12 per cent monocytes, which gave encouragement. The heterophil test first gave a positive result with a dilution of 1 to 24, but by the third week of her illness the result was positive with a dilution of 1 to 64. A positive result of a test with a dilution of 1 to 64 indicates a diagnosis of infectious mononucleosis, provided that the child has not received an antitoxin or horse serum within a year.

The children do not have anemia, as can be seen in this case. This child's red blood cells were above 5,000,000 per cubic millimeter. The platelet count was normal. The persistence of the distortion of the normal count in these children may go on for a considerable time. In some that I have watched a change in the relation of the granulocytes to the nongranular cells persisted for as long as six months.

Röntgenotherapy is not advisable for the same reason that chemotherapy is not—they are too depressing. Better results are obtained by the use of ultraviolet rays, when the concentrated type from a water-cooled quartz mercury vapor arc lamp can be used on the glands.

DR MERVIN C. MIERSON, Brooklyn. This subject is timely, and Dr. Grove has given a comprehensive and splendid presentation. Little has been written on this subject in the otolaryngologic literature. This disease is frequently encountered in a patient without enlarged cervical lymph nodes. I believe it is most important to be able to differentiate infectious mononucleosis from diphtheria.

I call attention to a fact which has been frequently mentioned among laryngologists, that is, any ulcerated lesion in the mouth or in the throat will yield Vincent's organism. I believe that most frequently the patients seen in consultation by the laryngologist are those who have been taken care of for a week or so by the family physician on the basis of a Vincent's infection because of the recovery of Vincent's organisms in smears.

An interesting and important fact to bear in mind is that patients with this condition have pain and soreness which is out of proportion to the duration of the disease and which is much more lasting and severe when compared to acute follicular tonsillitis or any other infection of that particular part of the throat. The manifestations of this disease are varied. One must not be misled by any textbook pictures of it.

DR WILLIAM E. GROVE, Milwaukee. Dr. Shea called attention to the persistence of glandular enlargement in cases of this kind. It is true that after the acute phase of the disease has disappeared the glandular enlargement may persist for many months. Also the heterophil antibody reaction will persist for a long time after the patient has recovered from the disease. Davidsohn found in one of his cases that the heterophil antibody reaction was still positive two hundred and ninety days after the cessation of the disease. The patients become greatly prostrated, and as the glandular enlargement and heterophil antibody reaction persist for a long time, so does the prostration. I noted particularly in the chart of Dr. Shea's case that the total white cell count was well within normal limits, so one must not be misled by the first white cell count which falls within normal limits but must insist on repeated differential counts.

The etiologic agent of this disease is not yet established, although it may belong to the group of *Bacillus monocytogenes hominis*.

Radium in Carcinoma of the Larynx DR SAMUEL SALINGER, Chicago

This article will be published in full in a later issue of the ARCHIVES

Urgent Surgery About the Head and Neck DR JOSEPH C BECK, Chicago

"Urgent surgery" is to be differentiated from "emergency surgery" and "choice surgery" By "urgent surgery" is meant that an operative procedure is definitely indicated and is to be performed as soon as an exact diagnosis has been established and the patient is fit for surgical treatment The time element is not designated but is within a week In contradistinction, "emergency surgery" is understood to be a procedure which must take place at once, whereas in "choice surgery" the procedure may or may not be done, although surgical intervention is clearly indicated for the benefit of the patient (An outline of the entire subject including all the "urgent surgery" in the domain of the ear, nose and throat was presented)

Demonstration of Color Photography of Diseases of the Larynx DR DEAN M LIERLE, Iowa City**Acute Infections of the Epiglottitis** DR JOHN MACKENZIE BROWN, Los Angeles

This article will be published in full in a later issue of the ARCHIVES

DISCUSSION

DR JOHN H FOSTER, Houston, Texas There is nothing I could add to a general discussion of this subject, but there is a point I want to stress, and that is the rapidity with which the symptoms develop in cases of inflammation of the epiglottis I recall 2 cases in which the patients complained of the first symptoms in the evening, the next morning the epiglottitis showed distinct evidence of abscess, and on the following day it was opened, with evacuation of a large amount of pus

Likewise, in certain cases of streptococcic infection of the epiglottitis the rapidity with which edema develops is astonishing I have seen large edematous masses develop in these cases which cause a great deal of dyspnea and require incision for the evacuation of the edematous condition

DR JOHN J SHEA, Memphis, Tenn When patients are brought into the hospital because of accidents with injuries to the neck, a roentgenogram assists in determining the air space, especially in the region of the epiglottis If there is beginning edema of that region, an ampule of calcium gluconate is given intravenously

For the acute infections insulin has been used, as suggested by Beale, and I believe small doses of insulin do have an effect in reducing acute edema in cases of this kind, especially in edema which is not streptococcic but which follows accidents

DR JOHN J BARNHILL, Miami, Fla One feature about this paper which I think needs even more emphasis than Dr Brown gave it is the connective tissue of the epiglottis I am convinced that laryngologists have given too little attention to connective tissue in the structures treated

In the epiglottis of Dr Brown's patient, as I understood, on the one side there was considerable connective tissue, on the other side there was none I take it that the side that had the connective tissue is the only side which had the abscess

DR JOHN MACKENZIE BROWN, Los Angeles There were abscesses on both sides

DR JOHN J BARNHILL, Miami, Fla On the lingual side there is considerable connective tissue, as any one will find out who dissects the epiglottis many times, and at the base of the epiglottis, namely, where it is attached to the hyoid bone, there is a large amount of connective tissue, and it is chiefly here that the abscess forms that is dangerous The laryngeal space is narrower there than at any other place, and the smallest amount of swelling will cut off the air

There are no abscesses in the neck, as I understand, except—and this may be disputed—where there is a considerable amount of connective tissue. One does not get an infection except where there is connective tissue. I believe that the connective tissue needs greater study than has been given it so far.

DR BURT R. SHURRY, Detroit. I should like to ask if sulfanilamide was used in the cases of streptococcal infection.

DR HARRIS P. MOSHER, Boston. It is old knowledge that one can remove the upper two thirds of the epiglottis with impunity. Let me give warning, however, if one has anything to do with the cushion of the epiglottis, then there may be trouble. Swallowing may be markedly interfered with.

DR JOHN MACKENZIE BROWN, Los Angeles. Sulfanilamide was used at first because on first examination it was feared that the condition was a streptococcal infection. The patient had been given the limit until the error in diagnosis was noticed.

Dr Barnhill, with regard to the connective tissue, I had 2 cases of abscesses on the laryngeal surface.

The first case I reported was that of a man who had been plowing. He thought that something hit him in the throat. What has been the predominating feature in all the cases is the sudden onset.

Influence of Tobacco Smoking on Health DR JOHN L. MYERS, Kansas City, Mo.

Smoking is an old social custom and is constantly becoming more popular. The mode, method and manner of smoking have changed. Constant smoking, moist tobacco and inhaling have created a health problem. Tobaccos differ in the content of nicotine. The cigaret is a scientifically produced article. Since the industry was established in America in 1872, cigaret smoking has constantly increased, during the last twenty years cigar and pipe smoking have decreased. Observations on tobacco smoke showed that smoke from moist tobacco contains more nicotine than from dry. The content of nicotine is increased by tightness of packing and rapidity of smoking. There are elements in smoke other than nicotine. The amount of nicotine absorbed depends on the manner of smoking. Nicotine and tobacco tar have morbid effects in cases of excessive smoking.

In susceptible people who smoke excessively the nicotine absorbed by the mucous membrane has an effect on

- 1 Cardiovascular system

- (a) increased heart rate
- (b) blood pressure raised by constriction of vessels
- (c) aggravation of angina pectoris
- (d) thromboangitis obliterans

- 2 Nervous system

- 3 Female organs

- 4 Special sense organs

Tar in tobacco smoke (a) irritates mucous membranes and (b) causes carcinogenic characteristics.

Dr Myers presented a study of the increase of pulmonary cancer since 1917 and amplified his paper with a number of slides showing (1) the increase in cigaret smoking up to the present, (2) the average nicotine content in various tobaccos, (3) the various other toxic products found in tobacco, (4) the nicotine content in various cigalets, (5) the increase in heart rate and blood pressure after smoking, (6) the effects of a filter, (7) the incidence of thromboangitis obliterans, (8) the size of blood vessels before and after smoking, (9) the effect of smoking on vision and hearing, and (10) the influence of tobacco on the increase of cancer of the lungs and of the pleura.

DISCUSSION

DR RALPH A FENTON, Portland, Ore This paper is entirely too well documented for comfort, and its facts, while they may be subjected to counter attack by researches subsidized by cigaret manufacturers, are not to be cast aside lightly Particularly is this true of Roffo's splendid experimental studies (Roffo, A H *Bol Inst de Med exper para el estud y trat d cancer* 15 377, 1938)

May I be permitted to contribute a case report on this subject? I had a patient about 60 years old who had smoked from ten to thirty cigarets daily for many years He had noticed an increasingly rapid heart rate for several years, with transient increases in blood pressure to 160 to 180 from his normal of 150 A professional man, he put in some time daily outdoors, smoking heavily at such periods Each winter for several years he suffered from an attack of rather severe acute tracheo-bronchitis, lasting several days He had a small amount of thick nasopharyngeal discharge each morning and commonly expectorated small amounts of rather thick tracheal mucus several times daily He did not inhale smoke deeply or blow it from the nostrils

Seven months ago he was incapacitated for three weeks by a severe auricular fibrillation, with a pulse rate of 120 to 160, requiring digitalis and rest in bed The blood pressure ranged from 170 to 190, and electrocardiograms were rather disquieting to his physician Complete cessation of smoking brought this man's pulse and blood pressure to normal within four weeks The nasopharynx and bronchi are clear His only present annoyance is an increase in appetite

One is too prone to accept the annoying accompaniments and sequelae of smoking because of the comfort and cheerfulness of its habitual use I am sorry Dr Myers is right but am grateful for his courageous message

DR JOSEPH C BECK, Chicago I think Dr Myers's paper had one statement in it which should be brought out, that is, that the effect of tobacco is an individual proposition, it is not uniform

I too am a sufferer from the toxic effects of tobacco Thirty-five years ago I had my first attack of auricular fibrillation, and since that time I have been afflicted more frequently, until in November 1939 when permanent auricular disturbance began It has not increased my blood pressure, but it has made me very uncomfortable at times with vertigo

In regard to cancer I observe cases of laryngeal carcinoma in various stages in my practice and have made a particular notation as to inhalation of smoke I believe that that is an important factor, that is, whether one inhales or does not inhale the smoke

DR HARRIS P MOSHER, Boston During the World War I was told that if I did not stop smoking I would be blind in ten years I am not blind now except to my own faults, and there are many others in the same condition I own up to a "cigaret cough" and a certain amount of "cigaret bronchitis"

Alcohol and tobacco have long been among the chief targets for reformers I was afraid that Dr Myers had joined this "long-haired" group It was a relief to find that he has not gone wrong yet The paper is an honest attempt to separate fact from prejudice The long bibliography shows that a large amount of work has been put on it

He narrows the problem at the start by saying that only some persons are harmed by tobacco, namely, those who are susceptible, and gives ample proof, most of it scientific, to substantiate this statement If now he would only give the figures showing how many people are susceptible his paper would be complete and so much more valuable Only this knowledge will tell us how much of a sinner tobacco is It is entirely an individual question with tobacco, as with alcohol, how much harm it does With each drug each person has to settle the question for himself In gaining this knowledge both drugs can and have humiliated many of us

In these days of allergy consciousness every one finds something which disagrees with him, even milk, nature's first and universal food, can be toxic Water alone has an unblemished record

Tar and nicotine are the two harmful ingredients in tobacco, but one author, McCormick, quoted by Dr Myers, named a most formidable list of by-products, the very names of which are frightening

The literature on this subject is voluminous, and one can pile up a large number of articles for and against the use of tobacco, the early articles of the opposition seldom being fully scientific

The innocent-looking cigaret has the largest nicotine content and therefore, by inference, is the most harmful. This is too bad, because the cigaret is the neatest and cleanest way to take tobacco. There is a sociability about a cigaret which a pipe lacks. No one would ever borrow your pipe, and you cannot pass a pipe around, like a pipe of peace, not in these hygienic days.

It helps and sometimes it is necessary in the evaluation of a medical article to know the author. Of the many men quoted by Dr Myers, I happen to know Dr Paul White. He is on the staff of the Massachusetts General Hospital and has specialized in diseases of the heart for many years. He feels that tobacco has no harmful effect on the heart. Experiments show that tobacco increases the pulse rate and slows the circulation in the finger tips and in the toes, but these regions are far from the vital centers of the body. In the literature it is stated that women are more prone to have bad effects from tobacco than men, sterility and miscarriage having been laid to it.

I do not believe that the apparent increase of cancer of the lung is due to smoking. Better methods of diagnosis explain it.

Since the time of Sir Walter Raleigh it has been known that tobacco has a calming effect on the nervous system. This action of tobacco should be a godsend in these nervous times.

DR HOWARD C. BALLENGER, Chicago. I have been particularly interested in the local rather than the systemic effects of tobacco smoking. In 200 or 300 young medical students, I was unable to determine that the amount of smoking had any visible evidence of local disturbances, that is, of irritation in the pharynx or in the nose. This may not be true in adults or in persons who have smoked a long time. By local evidence I mean redness, inflammation or hypertrophy of the lymphatic tissue. There seems to be no correlation between the amount of smoking and these observations. The absence of redness may possibly be due to the vasoconstricting action, which I think all investigators now agree is caused by tobacco smoking, that is, peripheral vasoconstriction.

Incidentally, in looking up the literature of recent years on this subject, I have come in contact with reports of the systemic effects and the most recent article I found was by Mulinos and Shulman (*Ann J M Sc* **199** 708 [May] 1940), who studied the vasoconstricting action of tobacco smoking. They found that it only lasts, as Dr Myers stated, about fifteen minutes. They measured the hand volume accurately, using both the denicotinized and regular cigarets, and found that there was no variation in the vasoconstriction. They found that inhaling the smoke prolonged this action, as has been brought out, but also found that deep breathing would produce the same effect. However, the latter finding has not been confirmed, as far as I know, so it may not hold. Filtering the smoke through cotton soaked in ferric chloride seemed to obviate this vasoconstriction. Cube cigarettes also had this effect.

When one tries to measure or to determine the effects of tobacco smoking one cannot be sure just what produces the harmful systemic effects. Nicotine is generally conceded to be a most important element from the standpoint of carbon monoxide. Should this thought be discarded? Dr Myers did not stress that, but it is stressed in the literature many times by investigators. The pyridine bases and ammonia, that is, the tars and aldehydes and particularly the ammonia, more often have a local action than a systemic effect.

In the literature three general actions seem to be the most important: first, the action on the central nervous system, secondly, the effect on the ganglions of the sympathetic nervous system and, thirdly, the action on the nerve ends of the voluntary muscles. This last-mentioned action is primarily stimulation followed

by paralysis, but the investigators whose reports I have read seemed to think that smoking is no factor in the latter condition, as there would not be sufficient nicotine to affect the nerve ends to any physiologic extent

In a summary of the possible systemic effects, perhaps one of the most important factors which has been mentioned and stressed—but which should be stressed again—is the desensitization factor. This factor probably has to be present to produce deleterious effects

Dr Mosher asked about some statistics. I did see one article on which I have made some notes giving statistics on the effects of tobacco smoking on the heart. Graybiel, Ashton, Starr and White, in the *American Heart Journal*, I think in 1932, gave statistics on a limited number, perhaps not enough to be of value, but increased heart rate seems to be present in at least four fifths of the smokers in this group. Blood pressure is increased in about two thirds of the group, that is, the average blood pressure is increased about 13 mm of mercury. The decreased T wave, which may simulate coronary disease, which seems to be due to tobacco as recently brought out, occurred in less than half, that is, in this particular group. I think this was a group of heavy smokers and that fact frightened a great many of them. This T wave decreased a third or a half from normal for thirty minutes to an hour. If heavy smokers have an electrocardiogram taken this effect will show up after smoking heavily.

DR JOHN L. MYERS, Kansas City, Mo. I have not found in the literature that there was any particular effect from removing part of the nicotine, only a part of it can be removed. The best filters take out only a little over half the nicotine and less than half the tar.

The Interrelations of the Ductless Glands and Otolaryngology DR WESTLEY M. HUNT, New York

(This paper embraced an analysis of the studies of the effect of the secretions of the ductless glands on the ear, nose and throat and also the effect of otolaryngologic involvement on the balance of endocrine functions. A discussion of the glandular interrelations, known and plausible therapy, supplemented by theoretic possibilities of the application of this interrelation was included.)

Dr Hunt presented a consideration of the advisability of surgical procedure under given endocrine manifestations and thoughts as to overenthusiasm in such therapy, as well as the complete ignoring of its possibilities. He also discussed a consideration of the physical, laboratory and roentgenographic manifestations which aid in diagnosis and influence prognosis.)

DISCUSSION

DR JOHN F. BARNHILL, Miami, Fla. Otolaryngologists have not given much attention to certain symptoms of enlargement of the pituitary gland.

I have recently had the opportunity of going over a great many pathologic specimens from persons who had apparently died from pituitary disease, and I was amazed in looking at the records to see how few were the local symptoms which one would expect to find in a patient who had died from that ailment. For instance, the pituitary is surrounded by certain nerves, the second, third, fourth and sixth. Involvement of the second, it is understood, causes very early symptoms of blindness.

It is important to point out that the optic chiasma does not always occupy the same position in relation to the pituitary. The chiasma may be far back and it may be forward. If it is far forward, the pituitary may not cause any ocular symptoms until late. If the chiasma is further back and over the center, the symptoms will occur early, for it would be under the highest part of growth.

The feature which amazed me most in the specimens which I examined was that as the growth enlarged, these nerves were stretched to a great extent. For instance, I found a specimen in which the seventh nerve had been stretched enormously, almost shredded, yet in the history of that case there was little facial palsy.

However, if one studies the symptoms as they arise from the various conditions which have been described this morning, it would be of great help not only in the treatment but also in diagnosis

Indurative or Myalgic Headache DR ERNEST M SEYDELL, Wichita, Kan

This article will be published in full in a later issue of the ARCHIVES

DISCUSSION

DR FREDERICK T HILL, Waterville, Maine Last year, as I recall, a noted authority on headache was a guest speaker and could tell us little about its mechanism Today Dr Seydell confines himself to one type of headache, one which is easily overlooked and attributed to other causes Perhaps, one of the most valuable thoughts brought out by this paper is the need for caution in always attributing headache to sinusitis One is so apt to be sinus minded when confronted with headache that, just as the ophthalmologist can always find a refractive error, the otolaryngologist thinks it must be due to sinus disease Yet there are many other possibilities which must be kept in mind

In many cases myalgic headache is not recognized as such but is diagnosed and treated as an allergic or endocrine condition The susceptibility to cold naturally suggests hypothyroidism I observed a typical case in which there were severe symptoms Infiltration with procaine hydrochloride gave entire relief temporarily Later an orthopedic surgeon made a diagnosis of cervical arthritis, and now the patient is being treated by having his neck stretched in some horrible apparatus suggestive of the medieval rack

As yet I cannot accept this myalgic headache as a clinical entity Rather it seems to be a syndrome—like Meniere's disease—presenting headache, nodes, spasm and painful areas in the muscles of the neck, and, as brought out by Dr Seydell, lowered local temperature Dr Seydell's theory of the mechanism involved in this condition appears logical The postural muscles of the neck are exposed to changes in temperature Cold induces vasoconstriction Because of some factor, as yet unknown, the cycle is not completed by vasodilation, and waste products accumulate in the muscles What is this unknown factor? As in so many similar problems, the answer seems to lie in the little understood autonomic nervous system It may well be that the successful treatment of this condition will be ultimately found in blocking of the cervical portion of the sympathetic trunk Perhaps the most practical thing to keep in mind is the importance of careful palpation of the neck in these cases of headache

DR RALPH A FENTON, Portland, Ore I am inclined to agree with Dr Hill that the condition reported is a syndrome rather than a definite clinical entity

I think that it might be well in looking over the question of so-called myalgic or indurative headache to consider the fact that this condition may be caused in two ways It may be caused by a reflex arc from the cold on the outside or by the sympathetic imbalance on the inside, and in that connection I recall some work carried out under the direction of Dr Larsell (Larsell, O, Barnes, J F, and Fenton, R A ARCH OTOLARYNG 27 266 [March] 1938) on the pituitary or the sella turcica and the sympathetic nerve connections of the sinuses, in which it was found that stimulation of the sphenopalatine region in rabbits produced a grossly visible ischemia of the blood vessels in the ear

Reasoning from that and from the work done on the cutting of the cervical sympathetics in these animals, it was figured that there was an arc which arose from the nasopharynx, from such regions as the back of the nose and the turbinates, and traveled down the sympathetic trunk and then out into the various cervical branches at the various levels of the neck It was referred to those cervical levels, each, of course, corresponding to certain muscles, and in that way was reflected up into the head and so through the reticulospinal tract and received in the thalamus, where all the pains are referred out through the particular cervical segments of the nerves, at which the faulty vasomotor impulse entered the sympathetic system and was then taken into the brain

I think that it will be found that Dr Larsell's interpretation, based on further work by Professor Allen of some years before (Allen, W F *Am J Physiol* 87 319 [Dec] 1928, *J Washington Acad Sc* 2 492, 1932), is explanatory and that the vasomotor imbalance accounts for all of these symptoms. It can work both ways, in and out.

DR BURT R SHURLY, Detroit. I should like to ask Dr Seydell if metabolism tests were performed.

DR GEORGE M COATES, Philadelphia. For years it seems that I have observed many cases of headache which would fall under this classification, whether it be a definite entity or not I do not know, but I am sure that I myself have definitely suffered from this type of headache. This is precipitated by two factors in my case. One is the cold draft on the back of the neck, which Dr Seydell has stressed, and the other is fixed posture, while I often have a stiff neck with myalgia, I do not often have a headache, but after a long day's work in the office with the head fixed in one position this headache comes on. At that time I find the muscles of the neck stiff. I have noted indurated nodules in the muscles of my neck, and on looking back, I remember that I have had these before.

As to the etiology of this condition, I do not know what it is due to. It is probably due to a great many factors, just as rheumatism in the broader sense is due to a great many factors. The experts on rheumatism will all tell you that it is not due to focal infection, but that focal infection plays a part, it is not all due to allergy for different foods or any one of a dozen different things, but it is a combination of all.

I think the treatment of this condition would be the treatment of rheumatism in general, that is, the elimination of all possible causes or factors.

With regard to the local treatment which Dr Seydell has used, I have not had any experience with that, but it seems ingenious. If it gives patients relief, it is a great advance.

I believe there are many cases of this kind, and the condition is often confused with sinus headache, to which Dr Seydell has drawn a parallel. For this reason, of course, it is important to make the differential diagnosis as Dr Seydell has suggested.

DR ARTHUR PROETZ, St Louis. Dr Coates raised the question of the nature of these nodules in stiff neck. I merely want to say that a long time ago Dr Sluder, working on "lower-half headache," noticed the nodules frequently. At one time he had the courage to take one out and have it examined, and it was a lymph node which showed absolutely no pathologic changes. This condition in these lower half headaches may have been analogous with the nodules described by Dr Seydell.

DR JOSEPH C BECK, Chicago. Knowing Dr Seydell's way of studying his subject and going over the literature, I am surprised that he did not go into the detail of Barany's investigative work on this subject. Dr Mithoefer and I were in Uppsala at the time when the professor was interested in this subject. He made extensive investigations on the pathogenesis of these nodules. An eminent neurologist, Hugh Patrick, followed by Pollock, in Chicago, from the neurologic side, preceded this investigative work but did not emphasize the edema, which was shown to be a chronic infiltrative edema in certain areas of the muscles which are subject to insults, and chilling was an important factor.

I have observed a few cases of this kind since my observations at Uppsala and bear them in mind. I recall a case, that of a dentist—Dr Seydell and Dr Coates have called attention to the factor of position in the causation of headache—who usually worked with a fan turned on the back of his neck or opposite to where he was working. Headaches would usually follow the turning on of the fan, when his neck was chilled. It was this plus the stretching and pulling of his muscles in that position which probably brought them on.

Dr Seydell's paper has brought out a good many things to think about.

Barany was later tremendously discredited when he brought the subject before the academy in Stockholm, because he made a statement that only one type of masseur could cure these conditions, namely, osteopaths. As you know, members

of this profession are prolific in that country. However, it seems that proper manipulation of these muscles has some benefit.

Another subject that I hope Dr Seydell will discuss is whether short wave therapy is beneficial.

DR EDWARD H CAMPBELL, Philadelphia. I should like to ask Dr Seydell to give more details of his injection technic and whether or not it helps in just a single attack.

DR THOMAS R GITTINS, Sioux City, Iowa. I cannot see how nodules or any changes in the muscles of the neck will bring about a real headache of the type which indicates at least some physiologic upset in the brain, meninges, ganglions or the nerve sheaths or cortical symptoms that come so commonly in headache.

I cannot see how those headaches would be due to reflexes from the neck any more than they can be thought to be reflexes from the sinuses and the eyes. Some local tissue reaction must be going on in the brain itself or in the meninges.

DR ERNEST SEYDELL, Wichita, Kan. I have no argument at all with reference to saying that this condition is not a clinical entity. I do not know what it is.

I know that myalgia of the muscles of the neck produces headache. I am sure of that.

Dr Hill spoke about cervical arthritis. A great many authors have spoken about the accompanying arthritis.

Kellgren (*Brit M J* 1 325 [Feb 12] 1938), in his work, has shown that a great deal of this pain may be referred to jaundice surrounding the particular muscle or, as in arthritis, that the pain is actually caused in the muscle.

In answer to Dr Shurly, metabolism tests have been made on a number of these patients. Some of the basal metabolic rates are low and some of them are high. I have found the condition in hypertensive cases. I do not think that information helps very much.

With regard to the blocking of the sympathetic nerve pathways, there are many physicians who claim that they can cure all headaches of this nature by blocking the ganglions in the nose, that is absolutely not true. The nodules cannot be changed and they will not disappear. Blocking the sphenopalatine ganglion does not stop the pain.

In regard to Dr Beck, I did not see the paper he mentioned. Halle (*Monatsch f Ohrenh* 45 768, 1911), I think, was the first otolaryngologist to bring this subject to the attention of specialists in this field, and he did a good deal of work on it.

There have been a number of physicians who have excised these nodes, and histologic changes have never been observed. If there are histologic changes, then the nodes in the muscles of the neck may be inflammatory. I have never heard of fever in any cases of this kind.

So far as massage is concerned, the condition cannot be cured by massage or any other treatment, even though the initial attack can be relieved. That is another good reason why binding edema does not mean much, because today a nodule will be present on one side and if some heat is administered to it, particularly early, it will disappear, and tomorrow another one will be on the opposite side. They are always changing, so I do not believe edema will be found when the nodules disappear.

Short wave therapy is of no more value than ordinary heat.

With regard to the technic of injection, the most important fact to remember is that injected procaine hydrochloride cannot help unless it is in the sensitive areas—and they are extremely sensitive. Something I forgot to state in my paper is that these nodes are never above the nuchal line, although the tender areas may be there. Injection of local anesthetic into the tender areas above the nuchal line does not usually give good results. Usually the results I have obtained have been from injections into the neck proper, and not much procaine is needed, from 15 to 2 cc of a 0.5 per cent solution. I do not use epinephrine.

The pain as I have described it—and I have gone into it rather thoroughly in my paper—is a muscular myalgia. It is similar to the pain associated with angina and with arthritis obliterans of the leg.

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Place Atlantic City, N J Time May 26-27, 1941

* Secretaries of societies are requested to furnish the information necessary to keep this list up to date

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PNEUMOCOCCIC MENINGITIS A REVIEW OF THE ENGLISH LITERATURE

WITH A REPORT OF TWO CASES IN WHICH THE DISEASE
WAS OF OTITIC ORIGIN

GOODLATTE B GILMORE, M D

AND

PHILIP SACKS, M D

NEW YORK

The varied chemotherapeusis of pneumococcic meningitis has been replaced by treatment with a single chemical, sulfapyridine, with beneficial results. Typing of the causative pneumococcus makes it possible to employ a specific pneumococcus serum, when that is available, instead of the polyvalent serums in wide use during the period of multiple chemotherapy. Specific serum administered early in conjunction with sulfapyridine, together with prompt and adequate surgical removal of the primary focus, has resulted in an increase in the number of recoveries. This will be still greater as knowledge and skill in serotherapy and chemotherapy advance.

While meningitis in the presence of an aural infection is most often secondary to the otitic lesion, it may possibly be due to paranasal sinusitis, especially sphenoiditis, or it may be transported by the blood from an infection in the respiratory tract or may even be a primary involvement of the meninges and not dependent on a demonstrable focus of infection in the fixed tissues. In treating meningitis it is obviously of the utmost importance to consider all the possible causes of meningitis as well as the infection in the temporal bone or paranasal sinus.

The division of meningitis into protective, or sympathetic, and suppurative is of value with respect not only to the prognosis but also to the therapy.¹ A protective meningitis is due to an infection adjacent to the dura, usually in the temporal bone or in a paranasal sinus. The immediate and complete eradication of such a focus of infection at

Read before the Bronx Otolaryngological Society, Nov 28, 1939

1 (a) Shambaugh, G E, Jr. The Surgical Treatment of Meningitis of Otitic and Nasal Origin, J A M A 108 696 (Feb 27) 1937 (b) Dwyer, J G Symposium on Otitic Meningitis, Laryngoscope 49 21 (Jan) 1939

the stage of meningeal irritation before the organisms penetrate the dura will probably forestall a suppurative meningitis. Procrastination in such a case enables the infecting organisms to overcome the resistance of the dura, invade the subarachnoid space and cause septic meningitis. The outcome then is not too certain, in spite of specific therapy. Surgical and supportive therapy may have to be more extensive.

In cases of suppurative meningitis early identification of the organism and typing, when the organism is a pneumococcus, are of the greatest importance. Sulfanilamide and sulfapyridine, the latter now in universal use, alter organisms, making the identification and typing difficult or impossible. This may deprive the patient of the aid of a specific biologic remedy, the therapeutic effectiveness of which is most marked when it is used early in the infection. If the cerebrospinal fluid system is not quickly sterilized and if walled off secondary foci occur, neither the chemical nor the biologic² agent will prevent death.

Of all the pneumococcic infections of the meninges, that caused by the type III pneumococcus is most often secondary to an otitic lesion and is most apt to terminate fatally. Review of reported recoveries from pneumococcic meningitis in the English literature reveals that reference to typing first appears in 1926. Reference to typing is found most often in reports of cases of meningitis following otorhinologic infections. Of 16 cases with recovery from meningitis due to the type III pneumococcus, in 12 the disease was secondary to an otitic lesion. A recovery from meningitis due to the type III pneumococcus and secondary to a sinusitis was not found. Of 113 cases with recovery from pneumococcic meningitis, including our own 2 cases, in 31, or 27.5 per cent, the meningitis was of otitic origin and in 6, or 5.3 per cent, it followed sinusitis. Table 1 is a summary giving the primary site of infection and the percentage of occurrence for each, as well as the type of pneumococcus and the frequency. Table 2 shows in decades the ages of the patients in whom these recoveries occurred and the number and percentage of cases for each decade. Of the cases of otitis, in 5 a mastoidectomy was performed before the onset of meningitis and in 16 after the onset of meningitis while in 10 no surgical treatment was given. Of the 6 cases in which the disease was secondary to a sinusitis, in 2 operation was done before the onset of meningitis, in 2 afterward and in 2 not at all. In 57.65 per cent of these cases the disease occurred in patients in the first twenty years of life. Before the advent of sulfanilamide and its derivatives the following drugs were used in these reported cases with recovery: ethylhydriocupreme hydrochloride, Pregl's solution, acriflavine, potassium per-

2 (a) Bullowa, J. G. M. The Specific Therapy of the Pneumonias, *J. Michigan M. Soc.* **38** 563 (July) 1939. (b) Baum, H. L. The Use of Specific Immune Serums in the Treatment of Streptococcic Infections, *Ann. Otol., Rhin. & Laryng.* **45** 969 (Dec.) 1936.

manganate, mercurochrome and methenamine. Various pneumococcic serums had been administered intravenously, intraspinally, subcutaneously and intramuscularly.

TREATMENT

A Prophylaxis—Kreutz and Witter,³ according to their report of 300 cases of acute mastoiditis in which a culture was made of material

TABLE 1—Data on Types of *Pneumococcus* in Reported Cases of *Pneumococcic Meningitis with Recovery*

Type of <i>Pneumococcus</i>	Primary Focus						No Primary Focus Evident	Totals
	Otitis	Anomalies of Sinuses	Pneumonia	Disease of Upper Res- piratory Tract *	Disorders Follow- ing Opera- tions on Nose and Throat †	Head In- juries and Results of Opera- tions on the Head		
I	2			2		2	2	9
II	1					1	2	4
III	12			1			3	16
IV	3	1	1	2		1		8
V	4							4
VI		1						1
VII		2	1			1		4
IX							1	1
XII							1	1
XIII	2							2
XIV						1		1
XVII	1					1		2
XVIII	1							1
XIX						1		1
XX		1						1
XXIII				1			1	2
XXV			1					1
XXVIII						1	1	2
XXXIX					1	1		2
XXXI		1						1
Typed	26	6	3	7	1	10	11	61
Not typed	5		12	10	2	1	19	49
Total	31	6	15	17	3	11	30	113
Percentage	27.5	5.3	13.3	15.0	2.6	9.7	26.5	

* Grip, influenza, sore throat and tonsillitis

† Submucous resection, turbinectomy and tonsillectomy

TABLE 2—Age Incidence for *Pneumococcic Meningitis with Recovery*

Age of Patient, Year	Number of Cases	Percentage
Less than 1	3	2.65
1-10	31	27.5
11-20	31	27.5
21-30	18	16
31-40	12	10.6
41-50	8	7
51-60	2	1.75
Not given	8	7

taken at the time of mastoidectomy, found pneumococci in 7 per cent of the cases. Of the 20 cases in which there was infection with the pneumococcus, in 16 the organism was type III. In 8 of these cases the

3 Kreutz, G. C., and Witter, G. L. Observations in Three Hundred Cases of Acute Mastoiditis, *Ann. Otol., Rhin. & Laryng.* 46:1060 (Dec.) 1937.

patient died, making a mortality of 50 per cent. The mortality from infection with *Streptococcus haemolyticus* was 4 per cent. The type III pneumococcus was 12 times as deadly as the streptococcus in complications of mastoid disease.

Goldman and Herschberger,⁴ in reporting a study undertaken in the attempt to determine the efficacy of active immunization against intracranial infections in cases of mastoiditis due to infection with the type III pneumococcus, stated that an autogenous vaccine made from a culture of material obtained from the mastoid at the time of operation reduced the mortality to 4 per cent making a mortality rate not higher than that reported by Kreutz and Witter for infection due to *Str. haemolyticus*. That not only autogenous vaccines but also serum raised resistance to meningeal infection caused by pneumococci as well as by other cocci was shown experimentally by Kolmer and Amano.⁵

No consideration of premeningitis therapy can be complete without thought of infections of the petrous pyramid and the labyrinth. That the labyrinth and the petrous pyramid can act as gateways for infection of the meninges is an accepted fact.⁶ Infection of these portions of the temporal bone fortunately gives ample warning. Besides, symptoms of meningeal irritation usually precede meningitis by a considerable period. Timely surgical drainage offers the only chance of preventing meningitis secondary to suppurative labyrinthitis and petrositis.

B. Sulfapyridine and Serum—MacIntosh and Whitby,⁷ in experiments on animals, showed that sulfapyridine inhibits cocci by causing loss of capsule and checking multiplication, it has no stimulating effects on the body defenses. Ross⁸ stated that pneumococci can acquire a tolerance or fastness to sulfapyridine in laboratory animals. He cited a case of fatal pneumococcal meningitis in which the organisms, at first sensitive to sulfapyridine, later became insensitive, as shown by cultures of material taken before and after the patient's death. This finding was corroborated by MacLean, Rogers and Fleming.⁹ These investigators found that different strains of pneumococci vary greatly in sensitivity to the chemical and also to the antibacterial power of normal

4 Goldman, J. L., and Herschberger, C. Prophylactic Vaccination Against Intracranial Complications Following Pneumococcus Type III Mastoiditis, *J. A. M. A.* **109** 1254 (Oct. 16) 1937.

5 Kolmer, J. A., and Amano, K. W. The Specific Prophylaxis of Pneumococcus and of Streptococcus Meningitis. II. Vaccine Prophylaxis, *Arch. Otolaryng.* **15** 547 (April) 1932.

6 Sacks, P. Hemolytic Streptococcus Meningitis of Otitic Origin. Report of a Recovery, *Arch. Otolaryng.* **28** 364 (Sept.) 1938.

7 MacIntosh, J., and Whitby, L. E. H. Mode of Action of Drugs of the Sulfonamide Group, *Lancet* **1** 431 (Feb. 25) 1939.

8 Ross, R. W. Acquired Tolerance of Pneumococcus to M & B 693, *Lancet* **1** 1207 (May 27) 1939.

9 MacLean, I. H., Rogers, K. B., and Fleming, A. M & B 693 and Pneumococci, *Lancet* **1** 562 (March 11) 1939.

human blood. They suggested that the primary dosage should be bold and that since the chemical is bacteriostatic only, a specific antibacterial serum or vaccine should be used at the same time. Fleming¹⁰ found that growth of pneumococci was completely restrained in defibrinated blood containing sulfapyridine and immune serum. When cultures were made of blood alone, of blood containing sulfapyridine or of blood containing immune serum, there was a growth of pneumococci. He advised that the patient be immunized to the highest degree possible.

May¹¹ treated with sulfapyridine a child suffering from pneumonia. Five days after the first dose of the drug, pneumococcic meningitis developed and the patient died. That the organism became tolerant to the drug is shown by the invasion of the meninges. Had the patient's resistance been supported by the use of serum in conjunction with sulfapyridine at the onset of pneumonia the meningitis might have been prevented. Bullowa¹² treated in rotation patients with pneumonia during the first four days of the disease, and reported the following death rates: for those treated with serum, a death rate of 12.3 per cent (57 cases), with sulfapyridine, 9.4 per cent (53 cases), and with serum plus sulfapyridine, 2.6 per cent (39 cases).

The antibodies, present in the blood normally or acquired as a result of vaccination or disease, do not enter the cerebrospinal fluid through the choroid plexus or the meninges if they are intact. In meningitis, however, a small amount of immune bodies can enter the cerebrospinal fluid¹³. Since antibodies have slight permeability through the meningovascular barrier and because the patient's own serum is less likely to cause an untoward reaction, Finland, Brown and Rauh (cases 68 through 73) administer the patient's serum intrathecally soon after the intravenous use of specific pneumococcus serum.

The absorption of sulfapyridine from the gastrointestinal tract being irregular and limited, administration of the drug should be supplemented by the use of sodium sulfapyridine intravenously, to maintain the concentration of the drug in the tissues at the desired level.

Experimental data and clinical observation emphasize the importance of augmenting the patient's immunity when sulfapyridine is given, so that the invading cocci may be destroyed before there has been time for tolerance to the drug to develop. Furthermore, by the combined use of the drug and the serum the doses of both may possibly be reduced with a lessening of toxic effects.

10 Fleming, A. Antibacterial Action In Vitro of 2 (*p*-Aminobenzenesulphonamido) Pyridine on Pneumococci and Streptococci, *Lancet* **2** 74 (July 9) 1938.

11 May, K. A Fatal Case of Pneumococcal Meningitis Treated with M & B 693, *Lancet* **1** 1100 (May 13) 1939.

12 Bullowa, J. G. M. Personal communication to the author.

13 Merritt, H. H., and Fremont-Smith, F. The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1937, p. 68.

C Blood Transfusions, Fluid Intake and Administration of Sodium Chloride—Blood transfusions should be administered early in the infection. Not more than 150 cc should be given at a time to adults and not more than 75 cc to children, at intervals of two to three days. How blood transfusions, aside from being ideal as supportive therapy, affect favorably the meningeal lesion is not known. Kopetzky¹⁴ stated that transfusions of whole blood during the stage of invasion tend to change toward normalcy the abnormal chemical findings in the spinal fluid. Sometimes, when the meningeal infection has not been of too long duration, blood transfusions aid in healing the lesions in the meninges, lessen the tendency toward blocking of the cerebrospinal flow and replace elements in the blood used up by the chemotherapy.

Patients who have recovered from severe pneumococcic infections are immune to the homologous pneumococcus for a variable period.¹⁵ That a pneumococcic infection causes a type-specific immunity has been corroborated in laboratory experiments.⁷ For infections of the blood stream, blood transfusions from immunized compatible convalescent donors are advocated as an ideal medical treatment.¹⁶ If specific donors are ideal for blood transfusions in treatment of infections of the blood stream, blood transfusions from such donors may prove just as ideal in treatment of infections of the cerebrospinal fluid system. Pneumococcus-type specific, compatible convalescent donors should not be difficult to find by means of study of the records of the general hospitals. It is hoped that this suggestion will stimulate investigation.

Ample fluid intake is essential to overcome the tendency to dehydration and to insure adequate cerebrospinal fluid for drainage. Sufficient sodium chloride should be administered to aid fluid retention by the tissues and perhaps help maintain a higher level of sodium chloride in the cerebrospinal fluid. Ample fluid intake is especially important in cases of pneumococcic meningitis, in which the tendency to block is more apt to occur, owing to a greater content of fibrin in the exudate.

D Surgical Therapy—Kolmer¹⁷ wrote

Septicemia is not due as much to multiplication of bacteria in the blood as to constant invasion by organisms proliferating in the primary and secondary foci of infection. Therefore, the first principle in treatment should be the establishment of the best possible drainage of these foci.

14 Kopetzky, S. J. The Diagnosis and Therapy of Otogenic Meningitis, *Pennsylvania M. J.* **42** 217 (Dec.) 1938.

15 Hamburger, M., Jr., and Ruegsegger, J. M. Early Recurrence of Sulfapyridine-Treated Type I Pneumococcal Pneumonia, *New England J. Med.* **221** 445 (Sept. 21) 1939.

16 Gill, E. G. Infection of the Blood Stream, *Arch. Otolaryng.* **27** 67 (Jan.) 1938.

17 Kolmer, J. A. Etiology, Prophylaxis and Treatment of Surgical Septicemia. A Discussion of the Principles Involved, *Arch. Otolaryng.* **26** 59 (July) 1937.

While no one is bold enough to advocate dispensing with surgical intervention for infection of the blood stream, there are such proponents for infections of the cerebrospinal fluid system. Those who are less insistent on surgical drainage of the primary focus are encouraged by the brilliant recoveries from meningitis which have resulted from chemotherapy. Some suggest that first the meningitis be controlled with these chemotherapeutic agents and that then the primary focus be drained. Others demand full clinical evidence of mastoiditis, including roentgenographic proof of bone necrosis. They overlook the fact that in the presence of meningitis the lesion in the mastoid process is overshadowed by that in the meninges. When meningitis is present the general symptoms of mastoiditis are hard to differentiate and the local signs are indefinite. In addition, the masking effects on the signs and the roentgen findings brought about by sulfanilamide and sulfapyridine make diagnosis difficult. It would seem that it is safer to operate if there is any doubt.

Meningitis following mastoidectomy may possibly be due to a breaking down of inflammatory barriers. However, when a meningeal invasion occurs before a mastoidectomy is performed, the barriers no longer act as a safeguard. The primary focus now acts as a base, with various routes leading to the meninges, along which the organisms may spread. Immediate and complete eradication of the primary focus and wide exposure of dura are indicated. This procedure, besides establishing drainage, removes such possible sources of infection as osteitic limiting plates and thrombotic venules, and enables the otologist to drain, or eliminate the possibility of, adjacent secondary dural foci.⁶ In the absence of a history or of symptoms of involvement of the labyrinth or petrous pyramid, nothing more need be done.

The English literature on cases of pneumococcic meningitis with recovery is reviewed in table 3.

In both cases of pneumococcic meningitis to be reported, recovery occurred.

REPORT OF CASES

CASE 1¹⁸—J. C. H., an 8 year old boy, was first seen on Feb. 1, 1939, at his home. He had a slight cold associated with pain in the left ear. The aural canal was found to be filled with phenoglycerin. When this was wiped out there was a trace of serosanguineous exudate as well as a moderately injected drum. On being questioned, the child admitted slight discomfort in the left ear. The right ear was normal. The nose and throat were congested. There was no headache or nausea, and the child appeared well. The temperature had not exceeded 99 F. On Feb. 3, 1939, the temperature was normal. On February 4 at 4 p. m. he had a sudden intense pain behind the left ear and a temperature of 104.8 F. The extremities appeared limp to his parents. The child, generally bright and vivacious, could enunciate only a few slurred and badly pronounced words. The skin was

18 From the pediatric service of Dr. L. H. Barenberg, Morrisania City Hospital.

TABLE 3—*Summary of Pneumococcal Meningitis with Recovery, as Reported in the Literature*

Case No	Author	Source of Infection	Age of Patient	Type of Pneumo coccus	Treatment
1	Parkinson, P J Brit J Child Dis 1 112, 1904	Pneumonia	2 yr	*	Spinal taps
2	Culper, R O M Rec 68 815, 1905	Primary	20 yr	*	Spinal taps
3	Cautley, E Diseases of Infants and Children New York, Paul B Hoeber, 1910, p 646	Primary	9 mo	*	Spinal taps
4	Cumming, J H Lancet 2 1294, 1912	Primary	12 yr	*	Spinal taps, pneumo coccus serum
5	Broadbent, W Brit M J 2 586, 1916	Broncho pneumonia	3½ yr	*	Spinal taps methen amine pneumococcus serum
6	Ibid	Grip	Adult	*	Spinal taps, methen amine, pneumococcus serum
7	Brown, A C Lancet 2 519, 1916	Primary	34 yr	*	Spinal taps, pneumo coccus serum
8	Royster, L T Virginia M Semi Monthly 22 4, 1917	Pneumonia	2½ yr	*	Spinal taps
9	Litchfield, L J A M A 72 1345 (May 10) 1919	Pneumonia	24 yr	*	Spinal taps, pneumo coccus serum
10	Ibid	Pneumonia	22 yr	*	Spinal taps, pneumo coccus serum
11	Ibid	Pneumonia	32 yr	*	Spinal taps, pneumo coccus serum
12	Ibid	Pneumonia	22 yr	*	Spinal taps, pneumo coccus serum
13	Ibid	Infection of upper respiratory tract	25 yr	*	Spinal taps, pneumo coccus serum
14	Gould, A G Boston M & S J 181 713, 1919	Broncho pneumonia	3 yr	*	Spinal taps, pneumo coccus vaccine
15	Horn, W S J A M A 80 1124 (April 21) 1923	Influenza	22 yr	*	Spinal taps, autoserum, pneumococcus serum
16	Campbell, J Lancet 1 54, 1925	Nasal operation cere brospinal rhinorrhea	16 yr	*	Spinal taps
17	Ervin, O E Atlantic M J 28 590, 1925	Primary	*	*	Spinal taps, pneumo coccus serum
18	Eichelbaum, H R Fifteenth Annual Report, United Fruit Co, M Dept 1926 p 105	Primary	24 yr	*	Spinal taps, spinal lavage, pneumococcus serum
19	Synge, V M Lancet 1 761, 1926	Fracture of cribriform plate	16 yr	IV	Spinal taps, autogenous pneumococcus vaccine
20	Roussel, A E Atlantic M J 30 159, 1926	Head in jury	40 yr	II	Spinal taps, methen amine
21	Ratnoff H L, and Litvak, A M Arch Pediat 43 466, 1926	Primary	7½ yr	III	Spinal taps, pneumo coccus serum, ethylhydro cupreine hydrochloride
22	Douthwaite, A H Lancet 1 1036, 1926	Primary	15 yr	*	Spinal and cisternal taps, pneumococcus serum
23	Simpson, A S Lancet 1 390, 1927	Primary	5 yr	*	Spinal taps, pneumo coccus serum
24	Globus, J H, and Kasanin J I J A M A 90 599 (Feb 25) 1928	Otitis	15 yr	IV	Spinal and cisternal taps
25	Harkavy, J J A M A 90 597 (Feb 25) 1928	Infection of upper respiratory tract	57 yr	I	Spinal and cisternal taps, pneumococcus serum

* The information was not given

TABLE 3—*Summary of Pneumococcic Meningitis with Recovery, as Reported in the Literature—Continued*

Case No	Author	Source of Infection	Age of Patient	Type of Pneumo coccus	Treatment
26	Carbonell, A, and Cook, E L Mil Surgeon 63 718, 1928	Fractured skull	21 yr	*	Spinal taps, optochin, pneumococcus serum
27	Croft, C R Lancet 2 700, 1928	Primary	26 yr	*	Spinal taps, pneumo coccus serum
28	Uhr, J S Arch Pediat 46 121, 1929	Pharynx	6 days	*	Spinal taps
29	Apfel, H Arch Pediat 46 516, 1929	Infection of upper respiratory tract	11 yr	IV	Spinal taps, pneumo coccus serum, Pregl's solution
30	Murphy R J Roy Army M Corps 52 293 1929	Otitis	22 yr	*	Spinal taps, modified radical mastoidectomy
31	Rohrbach, H O Penn sylvania M J 32 646, 1929	Pneumonia	5½ yr	IV	Spinal taps, pneumo coccus serum
32	Lynch, L J New En gland J Med 203 256, 1930	Pneumonia	16 yr	*	Spinal taps, pneumo coccus serum
33	Stroessinger, H N Brit J Child Dis 27 35, 1930	Otitis	5 yr	*	Spinal taps, mercurio chrome
34	Mella, H U S Vet Bur M Bull 7 77, 1931	Primary	Adult	*	Spinal and cisternal taps, Ringer's solution, irrigation
35	Amesse J W Colo rado Med 28 361, 1931	Infection of upper respiratory tract	17 mo	I	Spinal taps
36	Kolmer, J A J A M A 96 1358 (April 25) 1931	Pneumonia	25 yr	*	Spinal and cisternal taps, pneumococcus serum
37	Weinberg, M H J Nerv & Ment Dis 74 38, 1931	Grip	33 yr	III	Spinal taps, meningococ cus serum, potassium permanganate enemias
38	Shuller, E H J Okla homa State M A 25 137, 1932	Primary	36 yr	*	Spinal and cisternal taps, pneumococcus serum
39	Creagh, E P N J Roy Army M Corps 59 212, 1932	Primary	18 yr	*	Spinal taps, pneumo coccus serum
40	Clark, J G Lancet 2 1330, 1932	Primary	20 yr	*	Spinal taps
41	Cavenagh, J B J Laryng & Otol 48 237, 1933	Otitis	16 yr	III	Spinal taps, radical mas toidectomy, exposure of dura
42	McAuley J and Hilhard F M Brit M J 1 139, 1933	Primary	27 yr	*	Spinal taps, pneumo coccus serum
43	Ashmun, S H Ohio State M J 29 243, 1933	Tonsillitis	6 yr	*	Spinal taps, ethylhydro cupreine hydrochloride neutral acriflavine
44	Ibid	Pneumococcal abscess	7 yr	*	Spinal taps ethylhydro cupreine hydrochloride, neutral acriflavine
45	Ibid	Primary	6 yr	*	Spinal taps, pneumo coccus serum
46	Reveno, W S, and Mc Laughlin, N Ann Int Med 7 102, 1934	Injury to paranasal sinuses	20 yr	I	Spinal and cisternal taps, pneumococcus serum
47	Bedell, C C J A M A 102 820 (March 17) 1934	Sinusitis	42 yr	IV	Spinal taps, cisternal lumbar irrigations, transfusions dextrose intravenously
48	Kubie, I S Ann Otol, Rhin & Laryng 43 692, 1934	Otitis	35 yr	III	Forced spinal drainage, radical mastoidectomy

* The information was not given

TABLE 3—*Summary of Pneumococcic Meningitis with Recovery, as Reported in the Literature—Continued*

Case No	Author	Source of Infection	Age of Patient	Type of Pneumococcus	Treatment
49	Steinholz, R, and Gleich, M J A M A 105 795 (Sept 7) 1935	Otitis	7 yr	III	Lumbar and cisternal taps
50	Meyer, P R J A M A 105 1844 (Dec 7) 1935	Primary	5 yr	*	Spinal and cisternal taps, transfusions
51	Smith, H R J A M A 105 1845 (Dec 7) 1935	Infection of upper respiratory tract	43 yr	*	Spinal taps, pneumo coccus serum
52	Weil, C K Arch Int Med 57 514 (March) 1936	Fractured skull	28 yr	I	Spinal taps, pneumo coccus serum
53	Revenel, S T South M J 29 86, 1936	Disease in throat	12 days	*	Spinal tap
54	Baron, C Kentucky M J 34 302, 1936	Pneumonia	9 yr	*	Spinal taps
55	Norbury, F G M Rec 144 62, 1936	Infection of upper respiratory tract	59 yr	*	Spinal taps
56	Tripoli, C J J A M A 106 171 (Jan 18) 1936	Primary	32 yr	III	Lumbar and cisternal taps, replacement of spinal fluid by meningo coccus serum
57	Bennett, J F, and Meler, H J Wisconsin M J 35 630, 1936	Otitis	9 yr	*	Spinal taps, supportive therapy
58	Harris, C R, and Yenikomshian, H A Lancet I 143, 1936	Tonsillectomy	25 yr	*	Spinal taps, pneumo coccus serum, mercuriochrome
59	Caldwell, J R, and Byrne, P S Brit M J I 1204, 1937	Sore throat	16 yr	I	Spinal taps azosulf amide
60	Allman, C H Arch Otolaryng 25 653 (June) 1937	Otitis	15 yr	III	Spinal taps, radical mastoidectomy, labyrinthectomy
61	Mertins, P S, and Mertins, P S Jr Arch Otolaryng 25 657 (June) 1937	Otitis	13 yr	IV	Spinal taps mastoidectomy azosulfamide sulfanilamide
62	Basman, J, and Perley, M A J Pediat 11 212, 1937	Otitis	9 yr	V	Spinal taps, mastoidectomy, transfusions, sulfanilamide
63	Frankman, R W, and Stewart, J V Ohio State M J 33 1105, 1937	Otitis	5 yr	II	Spinal taps, mastoidectomy, transfusion
64	Mitchell, A G, and Trachsler, W H J Pediat 11 183, 1937	Otitis	*	V	Spinal taps, azosulfamide, ethylhydrocupreine hydrochloride
65	Neal, J B, and Appelbaum, E Am J M Sc 195 175, 1938	Sinusitis	*	XXXI	Spinal taps, sulfanilamide
66	Ibid	Nasal operation	*	XXIX	Spinal taps, sulfanilamide
67	Ibid	Otitis	*	IV	Spinal taps, bilateral mastoidectomy, sulfanilamide
68	Finland, M., Brown, J W, and Raugh, A E New England J Med 218 1034, 1938	Cerebellar exploration	19 yr	XVII	Spinal taps, sulfanilamide
69	Ibid	Compound fracture of frontal bone	8 yr	VII	Spinal taps, pneumo coccus serum
70	Ibid	Laceration in parietal region	17 yr	XXVIII	Spinal taps, sulfanilamide, transfusions, patient's serum intra spinally

* The information was not given

TABLE 3—*Summary of Pneumococcic Meningitis with Recovery, as Reported in the Literature—Continued*

Case No	Author	Source of Infection	Age of Patient	Type of Pneumo coccus	Treatment
71	Ibid	Otitis	10 yr	III	Spinal taps, radical mastoidectomy, exposure of dura, patient's serum intraspinally, sulfanil amide
72	Ibid	Head injury	7 yr	XIX	Spinal taps, pneumococcus serum, transfusions, patient's serum intraspinally
73	Ibid	Primary	13 yr	XXVIII	Spinal taps, sulfanil amide, pneumococcus serum, patient's serum intraspinally
74	Boyd, L J, Baron, B, and Schlachman, M New York M Coll & Flower Hosp Bull 1 99, 1938	Primary	48 yr	II	Spinal taps, pneumococcus serum, patient's serum intraspinally, ethylhydrocupreine hydrochloride, azosulfamide
75	Ibid	Primary	14 yr	II	Spinal taps, pneumococcus serum, patient's serum intraspinally, ethylhydrocupreine hydrochloride, azosulfamide
76	Young, F Brit M J 2 286, 1938	Otitis	5 yr	*	Spinal taps, sulfanil amide
77	Roberts, W Arch Otolaryng 28 140 (July) 1938	Otitis	17 yr	III	Spinal taps, mastoid revision, pneumococcus serum, transfusions
78	Gubner, J Arch Otolaryng 28 241 (Aug) 1938	Otitis	5½ yr	III	Spinal taps, sulfanil amide, mastoid revision, transfusions
79	Latto, C Brit M J 1 566, 1938	Primary	26 yr	I	Spinal taps, azosulfamide
80	Landon, J Brit M J 1 844, 1938	Primary	5 yr	*	Spinal taps, azosulfamide
81	Allan, W B Mayer, S, Jr, and Williams, R Am J M Sc 196 99, 1938	Fractured skull	16 yr	XIV	Spinal taps, sulfanil amide
82	Ibid	Operation for tumor of eighth nerve	42 yr	XXIX	Spinal taps, sulfanil amide
83	Ibid	Disease of frontal sinuses	18 yr	XX	Spinal taps, bilateral radical sinus operation, sulfanilamide, infusion, transfusions
84	Query, R Z J A M A 111 1373 (Oct 8) 1938	Broncho pneumonia	33 yr	VII	Spinal taps, pneumococcus serum, sulfanil amide
85	Robertson, K Lancet 2 728, 1938	Primary	14 yr	*	Spinal taps, sulfapyridine, polyvalent serum, soluseptasine (sulfanil amide derivative)
86	Reid, G C K, and Dyke, S O Lancet 2 619, 1938	Sore throat	7 yr	*	Spinal taps, sulfapyridine
87	Cunningham, A A Lancet 2 1114 1938	Primary	47 yr	I	Spinal taps, sulfapyridine, sulfanilamide
88	Cawthorne, T J J Laryng & Otol 54 444, 1939	Otitis	*	XVII	Spinal taps, sulfapyridine, pneumococcus serum
89	Patton, P B, Tittle, C R, and Wynne H K Internat Clin 2 255, 1939	Infection in upper respiratory tract	14 yr	XXIII	Spinal taps, bilateral mastoidectomy transfusions, sulfapyridine
90	Kreinlin, S Arch Otolaryng 29 371 (Feb) 1939	Disease in frontal sinus	20 yr	VII	Spinal taps, sinus operation, pneumococcus serum, sulfanilamide

* The information was not given

TABLE 3—*Summary of Pneumococcic Meningitis with Recovery, as Reported in the Literature—Continued*

Case No	Author	Source of Infection	Age of Patient	Type of Pneumococcus	Treatment
91	Applebaum, E Laryngoscope 49 30, 1939	Otitis	15 yr	XIII	Spinal taps, sulfanilamide, azosulfamide, transfusions
92	Ibid	Sinusitis	16 yr	VI	Spinal, clisternal taps, sulfanilamide, azosulfamide, pneumococcus serum, transfusions
93	Ibid	Sinusitis	20 yr	VII	Spinal taps, sinus operation, sulfanilamide, azosulfamide, pneumococcus serum
94	Ibid	Otitis	10 yr	I	Spinal taps, bilateral mastoidectomy, pneumococcus serum, azosulfamide, sulfanilamide
95	Silverman, D, and Thorer, M Arch Otolaryng 30: 431 (Sept) 1939	Otitis	47 yr	III	Spinal taps, sulfanilamide, transfusions
96	Hewell, B A, and Mitchell, A G J A M A 112 1033 (March 18) 1939	Otitis	8 yr	III	Spinal taps, mastoidectomy, sulfanilamide, ethylhydrocupreine hydrochloride
97	Ibid	Otitis	9 yr	V	Spinal taps, mastoidectomy, sulfanilamide, ethylhydrocupreine hydrochloride
98	Ibid	Otitis	10 yr	III	Spinal taps, mastoidectomy, sulfanilamide, ethylhydrocupreine hydrochloride
99	McAlpine, D, and Thomas, G C Lancet 1 754 1939	Head cold	24 yr	*	Spinal taps, sulfapyridine
100	MacKeith, R C, and Oppenheimer, G Lancet 1 1099, 1939	Infection in upper respiratory tract	28 yr	IV	Spinal taps, sulfapyridine, sulfanilamide
101	Ibid	Primary	30 yr	III	Spinal taps, sulfapyridine
102	Raman, P S Lancet 1 1101, 1939	Primary	34 yr	*	Spinal taps, sulfapyridine
103	Hodes, H L Gimbel, H S, and Burnett, G W J A M A 113 1614 (Oct 28) 1939	Pneumonia	34 yr	XXV	Spinal taps, sulfapyridine
104	Ibid	Otitis	7 yr	I	Spinal taps, sulfapyridine
105	Ibid	Otitis	11 yr	V	Spinal taps, mastoidectomy, sulfapyridine
106	Ibid	Primary	32 yr	IX	Spinal taps, sulfapyridine
107	Ibid	Primary	49 yr	XXIII	Spinal taps, sulfapyridine
108	Ibid	Primary	35 yr	XII	Spinal taps, sulfapyridine
109	Ibid	Otitis	45 yr	III	Spinal taps, sulfapyridine
110	Ibid	Otitis	11 yr	III	Spinal taps, sulfapyridine
111	Cavenagh, J B J Laryng & Otol 54 624, 1939	Otitis	17 yr	*	Spinal taps, radical mastoidectomy, subtemporal decompression, incision of dura, azosulfamide, sulfapyridine

* The information was not given

bluish white. He rolled his head from side to side and tried to shield his eyes from light. At 5 p. m. he had projectile vomiting. One of us (P. S.) again saw the child at this time. He appeared to be critically ill. He had alternately stupor and delirium. The left drum was intact, flat and not injected but gray. The right ear was normal. The throat was injected. Cerebral involvement was more marked than was meningeal. Dr. L. H. Barenberg, a pediatrician, was called in consultation. The provisional diagnosis was (1) encephalitis, (2) meningitis. The child was therefore sent to the pediatric rather than to the otolaryngologic service of the Morrisania City Hospital.

Examination on Admission—The temperature was 105.2 F. and the pulse rate 132. The skin showed marked tache cérébrale. There was no rash. The pupils were equal and reacted to light and in accommodation. There was early papilledema of the left eye. The right eye was normal. The neck was stiff. There was no adenopathy. The chest and abdomen were normal. Neurologic examination revealed palsy of the left facial nerve and left hemiparesis. He had a slight left lower abdominal reflex, all other abdominal reflexes were absent. The left cremasteric reflex was absent and the right present. He had a Babinski sign on the left side, and the Kernig sign was elicited on both sides, the Brudzinski sign was positive. The other deep reflexes were diminished. A spinal tap showed turbid fluid. The pressure was 300 mm. of water. It contained 1,200 cells (mostly polymorphonuclear) per cubic millimeter. Sugar was present and globulin increased. Smear revealed gram-positive diplococci. Culture of the spinal fluid for type XVIII pneumococci was later found positive.

A myringotomy on the left side revealed a dry middle ear without subsequent drainage.

Treatment and Course—Because sulfapyridine was not available, the patient was given 40 grains (2.40 Gm.) of sulfamidamide as an initial dose and subsequently 12½ grains (0.75 Gm.) every four hours with an equal part of sodium bicarbonate. A blood count showed 25,000 leukocytes with 92 per cent polymorphonuclears and 8 per cent lymphocytes. The value for hemoglobin was 86 per cent. Urinalysis, culture of material from the throat and culture of the blood gave normal results. The patient complained of severe headache and was restless. He took fluids poorly and was incontinent.

The next day he had marked nuchal rigidity and was stuporous. Because of vomiting he was given azosulfamide (disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3',6'-disulfonate), 20 cc. of a 2.5 per cent solution intramuscularly every four hours for three doses. Sulfapyridine was then obtained. Fifteen grains (0.90 Gm.) was given, followed by 7½ grains (0.45 Gm.) every four hours. Owing to insufficient fluid intake and vomiting an attempt at spinal tap resulted in no flow of cerebrospinal fluid. Cisternal puncture was considered. However, a clysis of 1,000 cc. of 5 per cent dextrose in physiologic solution of sodium chloride was followed by a spinal tap with satisfactory fluid flow. The reaction to the Mantoux test, roentgenographic appearance of the chest and results of the Kahn test were normal. A roentgenogram of the left mastoid showed a moderate cloudiness. There appeared to be absorption of trabeculae in the posterior group of cells.

On the morning of the third day the patient was less stuporous and showed definite improvement. The palsy of the facial nerve was less marked. He took fluids well, and the temperature came down to 100 F. A herpetic lesion of the right cheek developed.

The next day he was drowsy. The temperature ranged between 101.8 and 99.6 F. The hemoglobin content was 61 per cent. The consensus was then that a

mastoidectomy was indicated. After a transfusion, operation was performed. The mastoid cells were filled with a thin, turbid pus. There was no apparent loss of cellular structure. The inner table and the sinus plate were removed. Culture of material taken from the mastoid process was reported as revealing *Micrococcus tetragenus*. Two cultures of spinal fluid yielded *Pneumococcus* type XVIII.

The next day, the fifth day of meningitis, the patient's general condition was improved. The nuchal rigidity was less marked. He was given 20,000 units of type XVIII antipneumococcus rabbit serum intramuscularly. The spinal fluid was less turbid and contained 1,500 cells. Cultures of this and of specimens of spinal fluid taken subsequently were sterile.

On the sixth day he was given 20,000 units of serum and a transfusion, and on the following day the final dose of serum (20,000 units) was administered.

The spinal fluid obtained subsequently was clear, contained 39 cells per cubic millimeter and had a normal chemical composition. From then on the patient made an uninterrupted recovery and was discharged on Feb. 22, 1939, after a stay of eighteen days in the hospital.

Comment on Case 1—This child has remained well and shows no ill effects from the meningitis. His complete and uneventful recovery speaks well for the therapeutic measures used in this case. Surgical intervention stopped further invasion of the meninges. Sulfapyridine inactivated the pneumococci and prepared them for phagocytosis. Specific serum by augmenting the patient's immune forces helped in overcoming the toxic effects of the invading organisms and aided in their destruction. The transfusion replaced the blood elements lost as a result of the infection and the drug. The clysis overcame the dehydration and restored the flow of cerebrospinal fluid.

The levels of sulfapyridine in the blood ranged between 4.2 and 13.3 mg per hundred cubic centimeters. The levels of sulfapyridine in the spinal fluid ranged between 2.8 and 11.4 mg per hundred cubic centimeters.

*CASE 2*¹⁹—P. H., a man aged 35 years, was admitted to Morrisania City Hospital on April 15, 1939. His illness began with severe right frontal headache and fever on the morning of the previous day. The headache became worse as the day progressed. He felt as if his head would split. He was not nauseated. He had anorexia and took fluids only. He had had a discharge from the right ear for five years. The ear felt the same as it always had. There was no pain, and the discharge was unchanged. On the day of admission, at 10 a. m., he lost consciousness. He does not remember anything of the following seven days, during which he was usually in coma.

Examination—Physical examination showed the patient to be comatose, he was restless and resisted examination. The pulse rate was 60 and the respiratory rate 36. The temperature was 105 F and the blood pressure 110 systolic and 60 diastolic. Examination of the fundi revealed tortuous dilated veins. There was moderate swelling of the right eyelids. The lungs, except for a few crepitant rales at the bases, were essentially normal. The left ear was not involved. The right ear showed evidence of chronic involvement, without signs of an acute exacerbation.

¹⁹ From the otolaryngologic service of Dr. G. B. Gilmore, Morrisania City Hospital.

In neurologic examination no deep reflexes were obtained. There was no Babinski sign. The abdominal reflexes were absent. There were a positive bilateral Kernig sign and a moderately stiff neck.

Lumbar puncture revealed cloudy fluid under increased pressure. Examination of the spinal fluid showed an increase in globulin, a total absence of carbohydrate and a cell count of over 1,000, the cells being mainly polymorphonuclears. A smear showed occasional gram-positive cocci.

Roentgenograms disclosed complete absence of cells in both mastoids. On the next day the laboratory reported the organisms to be either streptococci or pneumococci, on the basis of smear examination. An endaural radical mastoidectomy on the right was performed the same day. A sclerotic bone with complete absence of cells was found. The aditus and the middle ear contained granulations and serous exudate. The bone in the region of the aditus was soft. Limiting plates were normal. The next morning there was complete paralysis of the right facial nerve, which cleared before the cavity made by the radical operation epithelized.

Treatment and Course—Since the infection was believed to be caused by *Str. haemolyticus*, the patient was given a preliminary dose of 75 grains (4.5 Gm.) of sulfanilamide with sodium bicarbonate. Sulfanilamide therapy was continued, 15 grains (0.90 Gm.) by mouth and 15 cc. of azosulfamide in a 5 per cent solution intramuscularly being given every four hours. The sulfanilamide was at times administered by gavage because the patient would not swallow. This dosage was continued from April 15 to 20. Also, on two occasions, 20 cc. of 5 per cent solution of azosulfamide was given intrathecally because of the patient's desperate condition. Dextrose was continuously administered intravenously to offset the tendency to dehydration.

The coma deepened during the first few days after operation, and on April 20 the patient appeared to be dying. He was unconscious and cyanotic, and the face, especially around the mouth, was covered by a herpetic rash. The temperature was 104.2 F. The night before, the temperature was 106.8 F., the highest during the illness. He could not be aroused from coma. The chemotherapy was discontinued. The temperature dropped by crisis and was normal in forty-eight hours. The next day the coma receded and the rash and cyanosis began to clear. The patient became brighter and on April 22 was fully conscious and fed himself, from then on he made an uneventful recovery. Evidently the chemotherapeusis, forced in this case because of the patient's desperate condition, was at least partly responsible for the continuance of the fever and coma.

Examination of the spinal fluid on April 16 revealed 4,150 cells, of which 76 per cent were polymorphonuclears and 24 per cent lymphocytes. Dextrose was absent, and the protein value 3 plus. On April 25 three specimens of spinal fluid, taken on April 17, 18 and 19 respectively, were successively reported as revealing type XIII pneumococcus. Difficulty in identification and typing of the organism caused this late laboratory report. Cultures of spinal fluid from April 19 on gave negative results, and the chemical and cytologic findings returned to normal. Spinal taps were done daily until April 26. Cultures of the blood were negative.

CONCLUSIONS

The division of meningitis into protective and suppurative is of value in relation to prognosis and therapy.

The diagnosis of bacterial meningitis should be made only on demonstration of the organism in the spinal fluid by means of culture. Early

identification of the organism and typing when the organism is a pneumococcus are of great importance

The incidence of meningitis complicating acute mastoiditis due to infection with the type III pneumococcus can be minimized by an autogenous vaccine made from a culture of material obtained from the mastoid process at the time of operation

Timely surgical drainage offers the best chance of preventing meningitis secondary to suppurative labyrinthitis and petrositis

The use of sulfapyridine and of specific serum are limited to a definite phase in the cure of pneumococcic meningitis. Sulfapyridine inhibits the growth of the organisms but does not destroy them. Specific serum helps the body forces, the clearing mechanism, involved in destroying the organisms and in neutralizing the evolved toxins. Chemotherapy and serotherapy combined will result in recovery when either of these methods alone may not

The chemical agent and the serum, especially the latter, are most effective when used early in the infection. If the cerebrospinal fluid system is not quickly sterilized and if walled-off secondary foci occur, neither the chemical agent nor the biologic will prevent death

Blood transfusions, ample fluid and sufficient sodium chloride should be administered as supportive therapy. In patients with a tendency to dehydration sodium chloride aids fluid retention by the tissues and perhaps maintains a higher level of sodium chloride in the cerebrospinal fluid

Blood that is type-specific for the pneumococcus and is taken from an immune convalescent compatible donor is suggested for transfusions

Surgical operation on the temporal bone or paranasal sinuses performed early with proper skill and knowledge may be the deciding factor between success and failure

A tabular resumé of 111 cases of recovery, gathered from the English literature, is given. Two cases of recovery from pneumococcic meningitis are reported, in 1 of which (the first of the kind to be reported in the English literature) the disease was due to type XVIII pneumococcus

NOTE—Since this paper was written Lewy²⁰ has reported cases of recovery from meningitis due to pneumococci of types XVIII, IV and III and has mentioned 6 other cases of recovery from meningitis of nonotitic origin

2940 Grand Concourse

1749 Grand Concourse

²⁰ Lewy, A. Report of the Chicago Committee on Otogenic Meningitis, 1939, *Arch Otolaryng* **31** 227 (Jan) 1940

PRIMARY MALIGNANT TUMORS OF THE TEMPORAL BONE

REPORT OF A CASE

H B STOKES, M D

OMAHA

Malignant tumors involving the middle ear cleft and the temporal bone are in no sense pathologic curiosities, nevertheless, they are sufficiently rare to present a most perplexing clinical problem. A number of excellent reports and reviews are available for reference in the literature, and many authors could be cited. The works of Furstenberg,¹ Keeler,² Schall,³ Robinson,⁴ Fraser⁵ and Scott⁶ are as noteworthy as any, but even these, though distinctly helpful, offer no definite solution to the problem in question. After a diligent study of the available literature one gains the impression that the management of malignant growths of the temporal bone is distressingly inadequate, that the prognosis is very grave, since early diagnosis is exceptional, and that the mortality rate remains almost unchanged over the years in spite of all modern facilities for diagnosis and treatment. One must admit that a number of extenuating factors exist which may in part explain this disquieting state of affairs, but these factors should not be accepted complacently as an excuse for failure, but rather regarded as a challenge toward development of further resources.

Before entering into the details of the following case report I offer a summary covering the salient points common to most malignant lesions of the temporal bone, with the feeling that in such a manner the interests

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1 Furstenberg, A C Primary Adenocarcinoma of the Middle Ear and Mastoid, *Ann Otol, Rhin & Laryng* **33** 677 (Sept) 1924

2 Keeler, J C Some Remarks on Otitic Malignancy, *Tr Am Laryng, Rhin & Otol Soc*, 1922, p 25

3 Schall, L A Neoplasms Involving the Middle Ear, *Arch Otolaryng* **22** 548 (Nov) 1935

4 Robinson, G A Malignant Tumors of the Ear, *Laryngoscope* **41** 467 (July) 1931

5 Fraser, J S Malignant Disease of External Acoustic Meatus and Middle Ear, *Proc Roy Soc Med* **23** 1235 (June) 1930

6 Scott, P, in discussion on Malignant Disease of the Ear (Including the Pinna), *J Laryng & Otol* **54** 576 (Sept) 1939

of the otologist may be better served than by resorting to a lengthy bibliographic review which merely paraphrases the writings of others. In preparing such a summary one unavoidably has to contend with a number of conflicting opinions which, though stimulating in argument, have no practical purpose in a short treatise. In order to arrive at a clearer conception of what is meant by primary malignant tumors involving the middle ear cleft and the mastoid and petrous portions of the temporal bone, all neoplasms occurring on the pinna and within the auditory canal external to the isthmus should be excluded. Moreover, neoplasms arising from the nasopharynx, the pterygomaxillary fossa, the sphenoidal recess, the parotid gland, the meninges and the brain substance itself cannot be considered in this classification. It must be remembered that the temporal bone may become implicated through continuity and extension from these regions, this results in manifestations which in some instances cannot possibly be differentiated clinically except by exploration or postmortem examination. Cases have been recorded in which the temporal bone became the site of secondary metastatic deposits from primary neoplasms arising in organs or structures far removed from the ear. In short, any neoplasm having a predilection for metastasizing to bone may do so to involve the temporal bone as a matter of coincidence. With these premises in mind it becomes obvious that because of anatomic difficulties the otologist may not be able to reach a diagnosis until the late stage of the disease.

The neoplasms most commonly met, in order of frequency, are the squamous cell carcinomas, the adenocarcinomas, the sarcomas and the hemangioendotheliomas. The age incidence seems to be much the same here as with malignant tumors found in other locations, the growth most often occurring in the middle decades of life, but not necessarily so, malignant disease of the ear has been seen in a child of 3 and in a woman of 94 years. Except for the histopathologic changes there are no reliable features which serve to distinguish one type of tumor from another. This observation applies equally to benign tumors and is of considerable importance, since what grossly might appear to be nothing more than an innocent polyp may on microscopic examination prove to be a highly malignant lesion. For some obscure reason as yet unknown, primary malignant tumors of the ear are very slow to metastasize, even the regional lymph nodes escaping until late in the disease, intracranial extension being the rule. Possibly the disease terminates fatally through intracranial extension before sufficient time has elapsed for metastases to develop.

Nothing pathognomonic can be attached to the early signs and symptoms of these tumors, in fact, they present themselves most often in disguise and simulate so closely the ordinary and common otitic afflictions that the otologist may be spared reproach if his suspicions are not

aroused until the intrusion of some puzzling or bizarre turn of events. A malignant growth can develop suddenly in an ear long affected with a chronic suppurative process or just as suddenly in an ear previously quite healthy. The onset may bear resemblance to a stubborn furunculosis, it may imitate acute purulent otitis media and mastoiditis. The initial diagnosis in a number of cases was some form of otomycosis, in other cases the patients were believed to have an otitic eczema. Chronic progressive deafness, both of the conductive and of the perceptive type, had been treated for many months, until some feature inconsistent with the diagnosis made its appearance. On several occasions labyrinthine disturbances had been recorded and some form of treatment instituted against one or more of the many causes of Meniere's symptom complex. Briefly stated, then, malignant disease may in the beginning mimic or supervene on a number of relatively innocent lesions involving those structures associated with the middle ear cleft and the more serious diseases of the mastoid and petrous portions of the temporal bone.

In analyzing a series of case reports collected from a variety of sources and tabulating those signs or symptoms which first led the physician to suspect that malignant disease might exist in any given case, it became apparent that his suspicions were aroused by one or more of the following clinical phenomena:

- 1 The presence of tough, resistant granulations or polyps and the rapid recurrence of these when removed by curettage or chemical means.
- 2 The appearance of a bloody discharge at the external meatus, sometimes spontaneous and at other times preceded by purulent otorrhea. This bleeding, though never much in amount, has a tendency to be obstinate and regular, once established.
- 3 A complaint of persistent deep-seated intractable pain about the ear, severe otalgia unexplained by any visible pathologic change in the tympanum, the posterior group of paranasal sinuses, the nasopharynx, the teeth or the larynx.
- 4 The occurrence of a supposedly commonplace lesion of the external or middle ear, not only becoming refractory to treatment but showing in its inexorable advance a baffling dissimilarity to the usual clinical course, finally producing complications inconsistent as to time and place.

The foregoing features, although not absolute criteria of malignant disease, are typical enough in their incidence and appearance to make it mandatory that the physician exhaust all the facilities at his disposal in order to establish the correct diagnosis at the earliest possible moment. A biopsy is the surest way of settling the issue, provided, of course, that gross material exists from which specimens may be taken during the early stages. It must be remembered, however, that histologic diagnosis is subject to error, therefore, it still is necessary to enlist the services of a competent neurologist or internist, as the case may demand, and ask the patient that he submit to a complete general examination, includ-

ing serologic, roentgen and other laboratory studies. If the patient will not consent to all these measures in every detail it would seem wiser to withdraw from the case entirely than to court disaster by procrastination and haphazard deductions, always and notoriously dangerous.

In the later stages the signs and symptoms are so pronounced that the diagnosis of malignant disease becomes almost self evident, so much so that one is able to predict with a fair measure of accuracy the probable situation and extension of the growth in and around the involved temporal bone. Pain on chewing is excruciating. Trismus is present and may develop into complete fixation of the temporomandibular joint. The regional lymph nodes become enlarged, and a visible swelling may occur over the mastoid process, in the temporal fossa or below the zygoma. Palsy of the various cranial nerves is often encountered, of the facial nerve most commonly and after that of the abducens and the oculomotor nerve. The jugular foramen syndrome of Avellis has also been noted, a simultaneous paralysis of the glossopharyngeal, vagus and spinal accessory nerves. Severe pain radiating along the course of one or more divisions of the trigeminal nerve occurs as a rule. The terminal stage is anticipated by neurologic signs and symptoms indicative of intracranial spread to the meninges, various centers in the cerebral hemispheres, the cerebellum, the pons and the medulla. Death is usually due to a generalized leptomeningitis, the result of contamination with pyogenic organisms.

In a sectional meeting of the Royal Society of Medicine, Colledge⁷ remarked that the clinical course of malignant disease in the temporal bone seems to be dominated by the fact that the dura offers an amazing resistance to penetration by the tumor, which spreads with relative ease through bone. Enormous destruction of bone can occur before the patient succumbs to some intracranial complication.

It can be stated without much fear of contradiction that there is no uniformity of opinion or technic in regard to treatment, nor can there be, since the disease, so complex in its ramifications, precludes standardization. The surgeon is often confronted with the necessity of modifying his operative procedure in order to cope with the pathologic findings in each case. Since most of the cases fall into his hands only after the disease has progressed into its later stages, surgical intervention, in order to accomplish anything, must be radical. It may be difficult at times to draw a distinction between the operable and the inoperable tumors, certainly from the results obtained, one is tempted to relegate the majority into the latter group. On the other hand, the surgeon faced with this desperate responsibility is motivated by

⁷ Colledge, L., in discussion on Malignant Disease of the Ear (Excluding the Pinna), *J. Laryng & Otol* **54** 596 (Sept.) 1939

the thought that something must be done, and quickly, so that suffering may be assuaged and life prolonged to some extent, though ultimate cure seems most unlikely. According to the best modern authorities, treatment consists of a combination of several methods now in use. Cutaneous incisions should be made preferably with the diathermy knife and all soft tissue excision with a suitable dissecting electrode. Portions of the tumor which for some reason or another cannot be removed should be destroyed with a coagulating current. A radical tympanomastoidectomy through the posterior route, not by the endaural, antauricular approach, is the operation of choice. The removal of bone must be extensive, in order to gain exposure and make access to the tumor as complete as possible. It is inadvisable to make a plastic skin flap, in fact, most writers advise a sleeve resection of the external canal, including the concha and the tragus. Amputation of the entire pinna has not gained favor. At the conclusion of the operation radium capsules are inserted into the depths of the radical cavity and radium needles implanted subcutaneously around the external ear. Post-operative high voltage roentgen therapy also is generally recommended.

REPORT OF CASE

Mrs. N. H., aged 63, in May 1929, coincident with an attack of influenza, had acute purulent otitis media in the right ear. The drum ruptured spontaneously, and the infection resolved without complications within two weeks.

January 1938. There had been no symptoms for a nine year interval, then the patient noticed the onset of slight deafness, associated with itching and a "crawling sensation" in the right ear. Since this itching became at times almost unbearable she consulted her general physician, who prescribed drops for the ear, diagnosing an otitic eczema.

April 1938. Itching was no longer prominent, but she experienced an occasional sudden sharp pain, radiating across the right side of the face. The right ear was more or less constantly affected by a dull ache, and the deafness seemed increasing. A high-pitched tinnitus was also present.

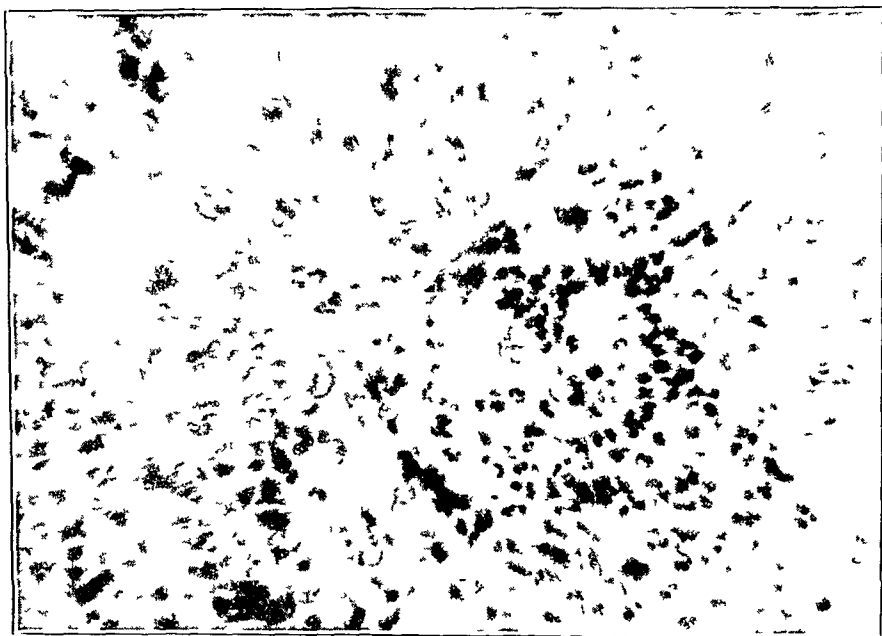
June 1938. The otalgia became progressively worse and was intensified by the act of chewing. Deafness was now almost complete. The patient consulted an otologist, who in turn referred her to a dentist. Two badly decayed and abscessed right upper molars were extracted, but without providing any relief.

July 1938. One morning about ten days after the dental extraction the patient noticed that her pillow was spotted with what appeared to be blood. Around the external meatus of the right ear dried crusts of blood were also seen. She immediately returned to her otologist, who diagnosed acute otitis media and prescribed irrigations followed by the instillation of some oily drops into the canal. The pain was somewhat relieved. A slight serous discharge, which at times was distinctly blood streaked, made its appearance. Several small frank hemorrhages occurred within the next two weeks, and the otorrhea became purulent and chronic.

September 1938. The patient complained of dull, diffuse headaches, especially on the right side above the ear. She suffered from insomnia, loss of appetite and loss of weight. The otalgia, which had subsided during the preceding two or three weeks, returned with increasing intensity. She was advised to undergo a mastoid-

ectomy but declined to submit to this. Instead, she consulted another otologist, who also advised operation, which was again refused. From this time on the patient turned to self treatment, irrigating the ear several times daily, applying heat, instilling a variety of proprietary ear drops into the canal and procuring relief from pain and insomnia by taking large doses of a number of sedative drugs which she obtained without prescription.

December 1938 The patient was first seen by me at this time, approximately eleven months after the onset of symptoms. It was difficult to obtain a coherent and complete history, since she was both mentally and physically in great distress. It became obvious that she was fearful of being told what she must have suspected, and the more she was questioned on the subject the more she resorted to evasions and contradictions.



Photomicrograph ($\times 500$) of biopsy specimen taken from the middle ear
Squamous cell carcinoma, grade 2

On examination the external canal of the right ear was partially filled with a foul-smelling purulent discharge. The skin of the canal was inflamed but showed no surface ulcerations. The greater portion of the drum was destroyed, only a small remnant remaining at the anterior inferior quadrant. A mass of "granulation tissue" protruded through this large defect in the drum. When touched with a probe this tissue seemed somewhat more firm than ordinary pyogenic granulations. The preauricular region was swollen, and another indurated swelling was observed below the mastoid process, extending about 2 inches (5 cm) downward along the anterior border of the sternomastoid muscle. Tenderness over the mastoid, though slight on palpation, was severe on finger percussion. Examination of the opposite ear, the nose and the paranasal sinuses gave negative results. No abnormalities were noted in the nasopharynx, throat or larynx. There was no paralysis of any of the cranial nerves. Roentgen examination of the mastoids showed in the right a most extensive destruction of bone. The cellular structure was replaced by a deep

excavation, which at first glance appeared as if a recent mastoidectomy had been performed. After much persuasion the patient consented to the removal of several small pieces from the granulomatous mass in the tympanic cavity for purposes of biopsy. Histologic diagnosis proved these to be portions of a squamous cell carcinoma of grade 2 (see photomicrograph).

The patient was referred to Dr. F. W. Niehaus for a complete physical examination. He reported favorably in regard to her general systemic condition, stating that no contraindications to operation existed. There was no clinical evidence of a primary neoplasm situated elsewhere than in the ear.

January 1939. The patient was admitted to the Methodist Hospital, Omaha, and prepared for operation, which was done under general anesthesia. A large curvilinear postauricular incision in the skin was made with a diathermy knife. Hemostasis was effected by a coagulating current. The attachment of the sternomastoid muscle was severed from the mastoid bone with a dissecting electrode. The cortex was exposed and removed with a gouge, and a radial tympanomastoidectomy was completed. During this step it was observed that the neoplasm had eroded and had excavated the entire mastoid process, leaving only a thin cortical plate. The tegmen mastoideum was destroyed by disease, exposing the dura of the middle fossa, which was covered with neoplastic tissue. This tissue on the dura was not removed, but coagulated. The tegmen tympani and the plate covering the sigmoid sinus were both intact. The tympanic cavity was invaded by the tumor, which had destroyed the incus and malleus and most of the drum. The base of the petrous portion in Trautman's triangle was necrotic, the horizontal and posterior semicircular canals standing out in bold relief. The swellings in front of the ear and below the mastoid tip were necrotic and friable and appeared to be lymph nodes greatly enlarged by secondary malignant deposits.

After the bone work on the mastoid, a complete sleeve resection of the concha, tragus and external auditory canal was performed. The initial incision, again made with the diathermy knife, started at a point slightly above and anterior to the tragus. This incision was carried through the intertragic fissure and followed closely the curve of the anthelix, encircling the cavum and cymba conchae, cutting through the crus of the anthelix and ending in front of the tragus. The skin and cartilage and all subcutaneous tissues included within this circular area were excised en bloc with a high frequency cutting current. All exposed soft tissues were thoroughly coagulated with a ball-tipped electrode.

Before the postauricular incision was closed, the operative cavity was lined with petrolatum gauze and loosely packed with the same material to provide a support for radium capsules. Four of these capsules, each containing 10 mg. of the element radium, were placed equidistant from each other and so distributed as to exert their influence on all four boundaries of the cavity. The capsules were left in place until a dose of 1,800 milligram hours had been received. At the same time radium needles were inserted by stab incisions in front of the ear in a fanwise manner and in the same fashion around the upper attachment of the sternomastoid muscle. Ten of these needles, each containing 2 mg. of radium, were left in place until an additional 1,800 milligram hours had been given. The total amount of radium therefore was 3,600 milligram hours. High voltage roentgen therapy was also instituted, the patient receiving in fractional doses a total of 656 roentgen units within the first postoperative week. She was discharged from the hospital after a stay of four weeks. The mastoid cavity was treated daily by cleansing irrigations, followed by the application of urea powder.

Her postoperative course for about six weeks was more or less uneventful. Pain was considerably relieved, and there was an encouraging improvement in her general condition.

March 1939 The patient complained again of severe headaches and recurrence of pain about the right ear. Relatives and friends noticed personality changes and loss of appetite and weight, insomnia was marked. At times for several hours she seemed irrational. On examination the operative cavity was clean except for a serous discharge. An area of devitalized necrotic bone, which appeared as if it might eventually form a sequestrum, was noted in the region of Trautman's triangle. A right-sided facial weakness was present, not sufficient to be called a true paralysis.

April 1939 All symptoms were much aggravated. The patient seemed declining rapidly and required frequent doses of opiates to relieve pain and induce sleep. A definite paralysis of the right seventh nerve involving the lower half of the face was noted, as the eyelid escaped, the paralysis was therefore a central supranuclear type. The left hand and arm seemed paretic. Intracranial extension to the right temporosphenoid lobe with involvement of the prerolandic motor area of the right cerebral hemisphere was apparent.

May 1939 The patient gradually became comatose, terminal generalized meningitis developed, and she died five months after operation.

CONCLUSIONS

To arrive at any definite conclusions on the basis of this case would be nothing short of fatuous presumption, since a single experience can furnish no basis for a claim to authority. This report is proffered, therefore, in the hope that it will in some small way add to the sum of knowledge already contained in the field of otology.

DISEASES OF THE SPHENOID SINUS

WITH REPORT OF A CASE OF CYST OF THE SPHENOID SINUS

EDWIN B. BILCHICK, M.D.

Assistant Otolaryngologist, Presbyterian Hospital
NEW YORK

The sphenoid sinus is the most posterior and the least accessible of the nasal accessory sinuses. This anatomic situation as well as the close proximity of the sinus to many vital and vulnerable structures has hampered knowledge of abnormalities there and has aroused in many otolaryngologists well justified caution in exploration of this sinus. In a paper in the *Laryngoscope*, "The Sphenoid on Parade,"¹ Cavanaugh gave credit to Dr. Cornelius G. Coakley for the first published papers on the significance and difficulty of diagnosis of sphenoid disease. With the improvement in instruments, lighting, roentgenograms and surgical technic, the sphenoid sinus has emerged from the unknown.

This paper will not attempt to encompass the knowledge of the embryology or anatomy of the sphenoid sinus or of the minute pathologic changes. Rather it will concern itself with the clinical pathology and symptomatology, especially as they are related to the neighboring structures. Particularly it will discuss the subject of retrobulbar neuritis, and a case of cyst of the sphenoid sinus with visual complications will be reported.

The embryology of the sphenoid sinus has been carefully described by various authors, including Schaeffer^{1a} and Hajek^{1b}. At birth it is only a faint depression in the cancellous tissue of the sphenoid body. At the third year it is the size of a pea. At the seventh it can really be made out as a sinus. The structure has been carefully worked out by Skillein,^{1c} Schaeffer, Hajek, Nevert² and others. The sinus borders on the orbit, optic nerve and its tracts, third, fourth and sixth nerves,

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From the Department of Otolaryngology of Columbia University and the Presbyterian Hospital Medical Center, Dr. John D. Kernan, Director.

1 Cavanaugh, J. A. Sphenoid on Parade, *Laryngoscope* 45:911 (Dec.) 1935.

1a Schaeffer, J. P. The Nose, Paranasal Sinuses, Naso-Lacrimal Passageways, and Olfactory Organ in Man, Philadelphia, P. Blakiston's Son & Co., 1919, p. 175.

1b Hajek, M. The Nasal Accessory Sinuses, St. Louis, C. V. Mosby Company, 1926, vol. 1.

1c Skillein, R. H. Accessory Sinuses of the Nose, Philadelphia, J. B. Lippincott Company, 1923, p. 369.

2 Nevert, H. Morphologic Variation as a Factor in the Symptomatology of Paranasal Sinus Diseases, *Arch. Otolaryng.* 1:366 (April) 1925.

middle turbinate, nasal septum, ethmoid sinus, nasopharynx, carotid artery, sphenopalatine ganglion, pituitary gland, meninges and brain. The anatomic relation of the sphenoid sinus to those structures and the subsequent pathologic sequelae are the basis of this paper.

PATHOLOGY

The pathology of the sphenoid sinus concerns chiefly acute, subacute and chronic infections, whether catarrhal, purulent, hyperplastic or allergic, as well as osteomyelitis, neoplastic disease and obstructions of the ostium. The normal sphenoid sinus is lined by a thin, delicate membrane of ciliated columnar epithelium, which may become much thickened and even polypoid as a result of infection. Acute purulent infection of the sphenoid sinus alone is a rare condition, which I have never encountered. Acute purulent sphenoiditis is almost invariably a concomitant of acute purulent pansinusitis and may result in osteomyelitis and meningitis. Acute exacerbations of a chronic infection are commonly met with, they may be purulent or catarrhal. The chronic sphenoid infections usually result in thickened membrane together with fibrosis, hyperplasia and often osteitis. Polyps may form, infiltration with eosinophils may occur in the allergic type. The secretion is usually scanty, even if purulent. Primary neoplasms are rare, although some have been reported, usually carcinoma. Secondary neoplastic involvement is frequent as an extension from the brain, pituitary gland, nasopharynx and adjacent sinuses. The malignant granulomas such as those in actinomycosis have been known to invade the sphenoid sinus. Cysts have occasionally been reported.³

SYMPTOMS AND DIAGNOSIS

The clinical symptoms⁴ of sphenoid sinusitis differ from those of maxillary frontal and ethmoid sinusitis in that the location of the pain is different, the findings are fewer, the discharge more elusive and the complications more varied. In general the diagnosis is more difficult. The pain is usually frontal, occipital or just behind the eye. It may, however, be referred to the mouth, at the junction of the soft palate and the anterior tonsillar pillar, to the vertex or to the mastoid process. The onset of pain may be sudden or gradual. It may be dull, throbbing, pounding, sickening, stabbing or burning. Other frequent complaints are malaise, sleeplessness, vertigo, tickling cough, postnasal drip, scabs in the pharynx, gastric disorders and diminished olfaction. When complications ensue there may be visual disturbances or paralyses. In cases of acute purulent infection, meningitis or cavernous sinus thrombosis may result. Examination may show little of importance. By direct anterior rhinoscopic examination and by posterior rhinoscopic examina-

³ Orr, E. Hemorrhagic Cyst of Sphenoid, *Laryngoscope* **44** 846 (Oct.) 1934

⁴ Ridpath, R. F. The Sphenoid Sinus, *Laryngoscope* **44** 657 (Aug.) 1934

tion with a mirror and even with the nasopharyngoscope, one may find little that is pathologic. The difficulties are tremendously increased by a large middle or inferior turbinate or by a deviated nasal septum. The secretion may be transient and scanty. If it is seen behind the posterior end of the middle turbinate, on the posterior end of the middle turbinate, in the sphenoethmoid recess or around the sphenoid ostium, sphenoiditis is suggested.

Roentgenograms⁵ are of material assistance in the diagnosis. Lateral positions as well as mentovertical positions should always be utilized. The Granger position may be used. The mentovertical position is taken with the patient prone and the extended chin on the roentgenogram. It shows the comparative structure as well as the pathologic condition of the two sphenoid sinuses. The lateral view not only shows the sphenoid sinus but gives the relation to the neighboring structures. It frequently leads to the diagnosis of cerebral, meningeal, pituitary and vascular lesions, besides revealing disease in the nasopharynx and in the other sinuses. Injection of iodized oil before the roentgenograms are made sometimes results in clarification.

Differential Diagnosis—Consideration of the differential diagnosis of sphenoiditis brings one into many obscure fields. Intracranial tumors and other lesions, especially of the pituitary gland, vascular aneurysms, migraine headaches, trigeminal neuralgia, multiple sclerosis, endocrine disorders and hysteria are only a few of the more important conditions which must be differentiated from sphenoid disease.

The diagnosis of mastoiditis or petrositis has been made in the presence of a running ear when the lesion really was purulent sphenoiditis. This error is illustrated by the following case, observed at Babies Hospital.

H. C., aged 9 years, was admitted to the hospital on Dec. 12, 1936, with a history of fever (temperature 103 F) and swollen neck of five days' duration and of unconsciousness for one day. Examination revealed a red, drooping canal wall together with swelling of the neck and parotid gland, as well as weakness in the lower part of the face. No pus could be seen in the nose. Roentgenograms showed no sinusitis, the sphenoid bone was not pneumatized. The mastoid antrum was hazy, and there was a profuse discharge from the left ear. A simple mastoidectomy was performed on the left but revealed no pathologic changes. Spinal tap yielded normal fluid. The next day pus appeared in the left naris. Death occurred the day after the child's admission. Autopsy showed acute sinusitis involving the left antrum and the ethmoid and sphenoid sinus, as well as an abscess cavity in the sphenoid sinus and cavernous sinus thrombosis due to *Staphylococcus aureus haemolyticus*.

TREATMENT

It is impossible in one brief paper to consider in detail the therapy of sphenoid lesions. The conservative management of sphenoid sinusitis

⁵ Law, F. M. *Accessory Sinuses Roentgenologically Considered*, New York, Paul B. Hoeber, Inc., 1933.

includes dietary and prophylactic measures, use of vitamins, especially A and B₁, diathermy, nasal shrinkage, nasal irrigations, suction irrigation, displacement by iodized oil or ephedrine and measures to open the posterior nares, including partial resection of the middle turbinate and submucous resection of the nasal septum. The sphenoid sinus may be irrigated with a cannula, or the anterior wall may be punctured with a trocar and irrigation performed with a cannula.

The operative procedures include removal of the anterior wall and perhaps the floor, local or general anesthesia being used. This removal may be done through the nares, with or without ethmoidectomy, or through the external route, usually after ethmoidectomy. These operations, together with elaborate amputation, have been carefully described by Skillern,^{1c} Hajek,^{5a} Sewall,^{5b} Ferris Smith^{5c} and others. The procedures are especially indicated in cases of asthma, bronchiectasis and retrobulbar and optic neuritis.

There is a group of too little discussed cases, in which headache, vertigo and malaise occur and in which little or no disease has been found in the sphenoid or other sinuses or anywhere else. In spite of exhaustive medical work-ups these patients have been afforded no relief. The headache in such cases is inconstant and not well localized. Many of these patients are labeled as hysterical. Yet removal of the middle turbinate, irrigation of the sphenoid sinus or removal of the anterior sphenoid wall relieves their symptoms. In some cases simple shrinkage with cocaine, epinephrine or ephedrine gives temporary relief. These are probably cases of vacuum sphenoid sinus. Otolaryngologists should hesitate before they dismiss these patients with headache as out of their province or as incurable. Empiric treatment should not be neglected.

VISUAL DISTURBANCES

The subject which I now wish to discuss is still the battleground of the ophthalmologists and the otolaryngologists—visual disturbances due to sinusitis, particularly retrobulbar neuritis and optic neuritis, so-called neuroretinitis.

It is important to differentiate these two. In both conditions one finds decreased vision, enlarged blindspots and shrinkage of the visual field. In neuroretinitis occur papilledema, engorged veins, distortion of contour, hemorrhages and inflammation. But, as Weill stated, retrobulbar neuritis is "a disease in which neither the patient nor the physician

5a Hajek,^{1b} vol 2, p 530

5b Sewall, E. C. Operative Treatment of Nasal Sinus Disease, *Ann Otol, Rhin & Laryng* **44** 307 (June) 1935

5c. Smith, F. Management of Chronic Sinus Disease, *Arch Otolaryng* **19** 157 (Feb) 1934

sees anything" An⁶ authoritative description of retrobulbar neuritis was given by Dunnington⁷ in the *Laryngoscope*, and I quote freely from his article The fundus is normal, and there is decreased vision with central scotoma The attacks are variable in severity and duration Many patients recover spontaneously, but others have permanent impairment of vision The causes of retrobulbar neuritis are numerous toxins, lead, arsenic, thallium, tumors of the pituitary gland and especially multiple sclerosis, of which retrobulbar neuritis may be the initial symptom even eight to twenty-four years before the other signs appear

Dunnington expressed the belief that rhinogenic retrobulbar neuritis is rare and stated that a rhinologist should insist on repeated tests of the visual fields before operating on patients with questionable intranasal disease, so that the possibility of an expanding intracranial lesion may be excluded White said he considered many more instances of retrobulbar neuritis to be due to tonsillar or dental infection than to anomalies of the sinuses The weight of opinion at present does not favor operation on the sphenoid sinus for retrobulbar neuritis But in many cases optic neuritis has been shown to be due to sphenoidal sinusitis⁸ In the near future I shall present a case of optic neuritis in which severe unilateral blindness was relieved by operation on the sphenoid sinus It is my opinion that when the sphenoid sinus shows disease or when no other cause can be found, optic neuritis should be an indication for sphenoidectomy⁹

I now wish to present a case of cyst of the sphenoid sinus, observed at the Presbyterian Hospital, Columbia University Medical Center, and reported with the permission of Dr John D Kernan, director of the department of otolaryngology, and of Dr John H Dunnington, director of the department of ophthalmology

REPORT OF CASE

C L, a man aged 52 years, was admitted to the ophthalmologic department of the Vanderbilt Clinic on May 2, 1939 with the complaint of diminished vision in the left eye for one month Two months before his admission he first noticed that the left eye felt different from normal A week before admission he noticed a dull ache in the eye, worse on moving it There was no family history of ocular trouble The patient's general health had always been good except for poor teeth In 1928 during a routine examination a 3 plus reaction to the Kahn test was

6 Weill, cited by Dunnington⁷

7 Dunnington, J H Etiology of Retrobulbar Neuritis, *Laryngoscope* **45** 685 (Sept) 1935

8 Suker, G F Ocular Symptoms, *Arch Otolaryng* **13** 764 (May) 1931

9 (a) Ramey, J V Bilateral Blindness Due to Affections of Posterior Accessory Sinuses, *Laryngoscope* **46** 185 (March) 1936 (b) Lemoine, A N Lesion of the Optic Tract, Probably the Result of Infected Sphenoid Sinus, *Arch Ophth* **20** 966 (Dec) 1938

found, and he was treated with bismuth for three years but was told that he was "Kahn-fast" He had worn glasses for reading for nine months There was no history of smoking or drinking

Examination on May 2, 1939 showed normal pupils The muscles were normal except for slight limitation of excursion in all directions, probably due to pain on motion The right disk was normal There was hyperemia of the left disk, associated with engorgement of the veins and slight blurring of the disk margin The visual fields showed an enlarged blindspot in the left eye Vision in the right eye was 20/15 and in the left eye 20/40 (fig 1)

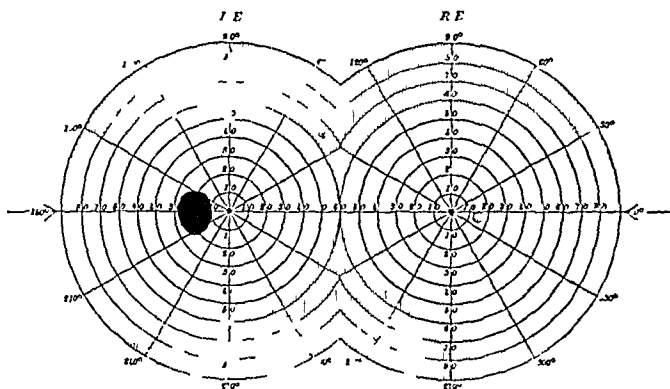


Fig 1—Visual fields (May 2, 1939) of the patient who had a cyst of the sphenoid sinus

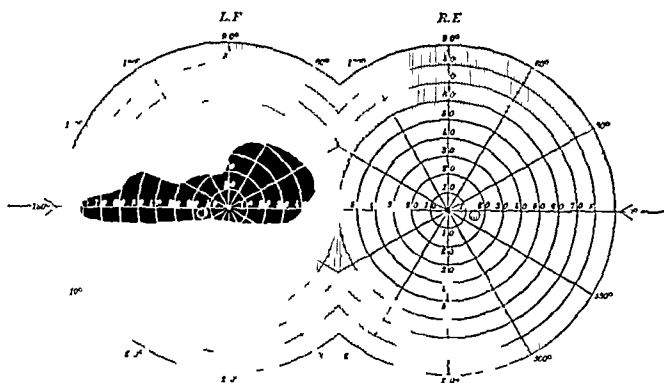


Fig 2—Visual fields of the same patient (May 8, 1939), showing decreased vision in the left eye with decided enlargement of the blind spot

Vision on May 8 had become rapidly worse, only light perception remaining in the left eye The fields showed marked concentric enlargement of the blindspot, with blotting out of most of the lower field (fig 2)

On May 11 the following report of examination of the nose was given by Dr George V Browne "The nares were normal On transillumination the left antrum was dark A probe was passed into the left sphenoid sinus I did not feel a normal posterior wall, it was thinner than it should have been It might be (?) advisable to open up the left sphenoid to see if there is any growth in it"

Lumbar puncture revealed normal fluid with no cells Results of the blood count were normal Neurologic consultation revealed nothing abnormal

On May 15 the patient was admitted to the Eye Institute of the Presbyterian Hospital. Lumbar puncture revealed normal findings. Tension of the eyes was normal. At this time the vision in the left eye was poor, sector defects extending from the upper and the lower periphery almost to fixation.

Roentgenograms of the skull, sinuses and orbits were reported on by Dr Pfeiffer. Stereoscopic roentgenograms of the skull showed the calvarium to be of average thickness, with normal convolutional impressions, vascular channels and sutures. The temporal bones were not well pneumatized and appeared somewhat sclerotic. The petrous ridges were equal, and the basal angle was normal. The sella turcica measured 11 by 13 mm and was involved anteriorly on the left side by a large defect, which included the sphenoid sinuses and the tuberculum sellae.

This defect extended posteriorly from the floor of the sella turcica across the sagittal plane to encroach on the right sphenoid and posterior ethmoid cells, anteriorly to the middle ethmoid cells, laterally to encroach on the left orbit and inferiorly below the ethmoid cells on the left side. The tuberculum sellae then was eroded through, particularly on the left side. The optic canal was divided vertically, an indication that the optic nerve must have been involved by pressure. The posterior half of the lamina papyracea was missing, and the mass must have been presenting in the nasal fossae. Definite margins of the defect could be made out at various points. The pineal body was calcified and was not displaced.

The frontal sinuses were of average size, the right one was clear and contained a small enostosis, which projected in from the inner frontal table, and the left was clouded. The right ethmoid cells and the anterior left ethmoid cells showed distinct cellular detail and appeared to be clear. The posterior left ethmoid cells were incorporated in the defect described, and this area was somewhat clouded. The antrums showed hyperplastic lining membranes. The left sphenoid sinus was included in the defect except for a small posterior recess under the sella. The right sphenoid cell was small and was encroached on by the lesion. The nasal fossae appeared clouded above. The right optic canal was normal.

The large defect described centered around the left posterior ethmoid cells and the upper recesses of the left sphenoid sinus, the impression was given, therefore, that the lesion must have arisen in one of these cells. The fairly definite margins suggest the possibility that this was a retention cyst, but carcinoma could not be excluded. It did not seem probable that the anomaly was an aneurysm, a pituitary adenoma or a meningioma.

On May 17 the patient was seen by Dr Dunnington, who made a diagnosis of neoplasm of the sphenoid sinus and suggested a biopsy.

He was transferred to the otolaryngologic division of the Presbyterian Hospital. Results of examination with the nasopharyngoscope were normal. On May 23 I explored the nasopharynx, with the patient under ether anesthesia. Some tissue on the right side of the nasopharynx was seen and felt, but it resembled adenoid tissue. It was removed for biopsy, but my conclusion at this time was that there was no neoplasm in the nasopharynx. This specimen, after biopsy, was reported as adenoid tissue.

On May 26, with the region under local anesthesia, the left sphenoid was explored. After shrinkage of the left naris with cocaine and epinephrine for one hour, the enlarged left middle turbinate was removed with a snare and a biting forceps. A few anterior ethmoid cells were curetted away. When an opening was made up into the sphenoid sinus a gush of yellow fluid (about 15 cc) spurted from the sinus. A large cystic membrane was felt in the sinus. The anterior wall of the sinus was removed with a biting forceps, and the cyst lining and entire mucous membrane were stripped from the sinus. As the whole operation was

practically bloodless, no packing was inserted, but bismuth subcarbonate powder was sprayed into the nares

The report on biopsy, submitted by Dr A P Stout, follows "Grossly the specimen consists of four irregular pieces of tissue Sections show lining of a cyst which is composed of three or four layers of rather compressed atrophic epithelial cells some of which are flattened and others cuboidal This rests upon a dense fibrous membrane which is continuous with the periosteum of the underlying bone There is a good deal of osteoid in the section indicating that there has been marked proliferation of the bony wall of the sinus The marrow spaces are filled by vascular fibroblastic tissue There is very little evidence of inflammation"

The postoperative course was smooth Vision rapidly improved On June 21 the vision was 20/20 plus 4 and the fields were practically normal (fig 3) The disk showed no residual effects from the papilledema except for slight pallor On June 13 iodized poppyseed oil was injected into the left sphenoid sinus Verticomenal and lateral roentgenograms showed the cavity to fill well The margins

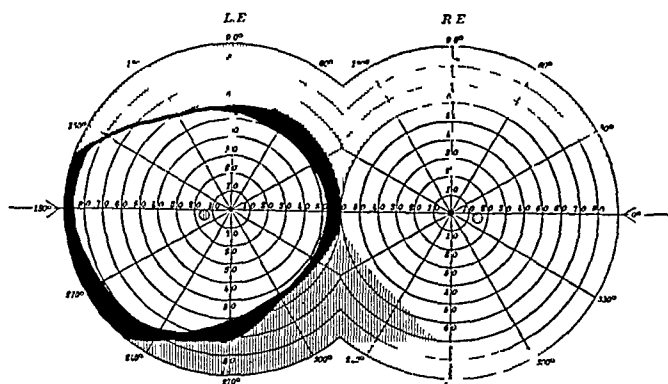


Fig 3—Visual fields (June 21, 1939) after operation, showing the vision to be practically normal

were smooth, there being no indentation suggesting polyps or marked thickening of the lining membrane

This case is representative of a lesion in the sphenoid sinus which resulted in extreme loss of vision and showed little on examination of the nose and nasopharynx but was diagnosed by probing of the sinus and by roentgen examination of the sphenoid sinus Vision was restored after a successful operation

SUMMARY

Because of its location and its relation to surrounding important areas, the sphenoid sinus is relatively difficult to approach and diagnosis is extremely doubtful at times Every diagnostic effort, procedure and instrument may be necessary to establish the diagnosis and to eliminate possibilities of other anomalies If no definite diagnosis can be made, one should not hesitate to explore the sphenoid sinus in suitable cases, as the vision may be at stake

PSYCHOLOGY OF THE LARYNGEAL FUNCTIONS

EMIL FROESCHELS, M D *

NEW YORK

The relation between the receptive and emissive functions of the larynx on the one hand and respiration and vocalization on the other are generally considered to be reflex. This point of view can be supported by considerable anatomic and physiologic data. The tenth cranial nerve, for example, which, as is well known, is closely connected with the parasympathetic nervous system, innervates both the larynx and the lungs. Irritation of regions supplied by the inner branch of the superior laryngeal nerve causes coughing. Coughing may be produced by stimulation both of the inner branch of the superior laryngeal nerve and of the branches of the vagus nerve in the trachea, in the lung tissues and in the pleura. It is well known that dangerous consequences may result from irritation of or injury to the recurrent nerve. Respiration may be partially or completely impeded. In cases of paralysis in the abduction position, vocalization may become difficult or impossible (Of the recent investigations on this subject, Réthi's¹ experiments on animals deserve special mention. Of further import in this connection are the therapeutic gymnastic exercises which I introduced to prevent the dangerous consequences of paralysis of the recurrent nerve.)

It is, however, pertinent to inquire whether the presence of the so-called conscious relations between the larynx and respiration or vocalization is not obscured by familiarity with these data concerning the reflex relations.

Gutzmann² emphasized the fact that, although respiration during speech is undoubtedly reflex, voluntary respiration also occurs. Many medical and pedagogic methods of improving the speaking and singing voice are based on breathing exercises, i. e., on voluntary influence on respiration during speaking and singing. Further, every one knows that a coughing spell due to a tickling sensation in the throat can be avoided by voluntarily breathing deeply or holding the breath.

This paper, however, is not concerned with these well known connections between conscious sensations in the larynx and the voluntary

* The author's name has sometimes been spelled "Froschels."

1 Réthi, A. Anatomisches Spiegelbild des Mechanismus der Taschenbandstimme und die Rekurrensfrage. III. Ueber den Schluckakt, *Monatschr. f. Ohrenh.* 69 130, 1935.

2 Gutzmann, H. *Physiologie der Stimme und Sprache*, ed. 2, Brunswick, F. Vieweg & Sohn, 1928, pp. 26-28.

acts which they may occasion. It is concerned with the possibility of the existence of heretofore unknown conscious sensations in the larynx. This question arose in connection with observations on patients with acute paralysis of the recurrent nerve. With respect to vocalization such persons may be divided into four different groups: (1) the completely aphonic group, (2) those who phonate in a breathy voice and with great waste of breath, (3) those who phonate with hypercontraction of the muscles ("Presstimme," or "pressure voice"), and (4) the group whose vocalization is in a high falsetto voice.

The last two groups will be considered first. It may be impossible to understand the peculiar behavior of the third type of patient, who, suddenly finding himself incapable of closing the glottis, "instinctively" innervates auxiliary muscles of the throat and mouth, producing a "pressure voice." But it is nevertheless valuable to emphasize the following fact. Such a patient, with no knowledge of phonetics and no conscious sensation of the closure of the glottis during normal vocalization, is suddenly able to make use of a substitute mechanism which certain phonetically trained physicians attempt to cultivate as a therapeutic measure. Does not this seem to indicate that something of the physiologic closure of the glottis becomes conscious even under normal conditions and that the functions which produce closure do not occur entirely unconsciously?

Patients with paralysis of the recurrent nerve, who immediately after the onset of the paralysis begin to speak in a high falsetto voice, will now be considered. During the production of high tones an oval or bottle-shaped opening of the glottis remains, even in the so-called phase of closure. This is to be accounted for, as is well known, by the high degree of tension in the vocal cords. Is it not possible that something of these physiologic processes penetrates into consciousness? And if so, does not this explain why the patient with the falsetto voice chooses that pitch which occurs under normal conditions when the glottis is not entirely closed?

As for the first type of patient, who has aphonia caused by paralysis of the recurrent nerve, it may be stated that if one accepts the train of thought just outlined, one cannot deny the possibility that these patients simply suspend every effort to vocalize when the normal closure of the glottis is no longer possible. This supposition is supported by the fact that many of them later learn to produce vocal sounds although the width of the glottis remains the same.³

In this connection two further sets of observations are pertinent, which I made on patients with acute laryngitis on the one hand and

3 Froschels, E. Ueber eine neue Behandlungsmethode der Stimmstörungen bei einseitiger Recurrenslähmung, *Monatschr f Ohrenh* 66 1316, 1932

with acute and chronic paralysis of the recurrent nerve on the other ⁴ Before I made my own investigations, Gellé observed the first-mentioned patients and noted respiratory disturbances. I was able to ascertain that the patients with acute laryngitis required a much more rapid rate of respiration in saying a prayer or in singing a little nursery song than is normally the case. Frequently the increase was so great that one was led to believe that the patient was helping himself voluntarily by means of respiration. Certain patients with paralysis of the recurrent nerve had normal pneumograms. Others, however, showed an increased rate of respiration, sometimes marked. The patients whose pneumograms were normal were, without exception, those who had had the paralysis for a long time, whereas those patients whose paralysis was of recent origin showed respiratory disturbances ⁵

At my ambulatory logopedic clinic in Vienna (Klinik für Ohren-, Nasen- und Halskrankheiten in Wien, Prof. Dr. H. Neumann) my former assistant, Dr. D. Weiss, for several years carried on investigations concerning the behavior of patients with normal voices and those with vocal disorders whom he temporarily deafened by the Lombard method (masking by means of noises) while they were singing. With Dr. Weiss's permission I shall use and interpret certain of his results for the purpose of this paper. He found a group of subjects who could keep unchanged the volume and pitch of tone which they were singing before the deafening began. Certain subjects in this group could even continue a song which they had begun before they were deafened, and sing it through to the end perfectly correctly. Since I myself was one of these subjects, I can report on the observations I made on my own experiences during the experiment. Immediately after the elimination of hearing, I distinctly felt the existence of my vocal cords. I even felt them to be in a certain state of tension. To the best of my knowledge I had this sensation for the first time in my life. Weiss reported analogous experiences on the part of a large number of subjects, some of whom maintained that they heard the tone they were singing, but, as Dr. Weiss stated, "one can clearly prove to the subject that he only feels it."

It seems obvious that the behavior just described is characteristic of the person with the so-called motor type of imagery. Weiss also stated this opinion, but he advocated a subdivision of this group of persons into those with the kinesthetic and those with the true motor type. The former possess a somewhat conscious feeling of movement

⁴ By these studies I have attempted to facilitate the difficult differential diagnosis between acute and chronic paralysis of the recurrent nerve.

⁵ Froschels, E. Ueber die Sing- und Sprechatmung bei akuter Laryngitis, *Ztschr. f. Hals-, Nasen- u. Ohrenh.* **13** 7, 1925.

and position, the latter do not have and probably do not need this conscious feeling. Weiss considers those of his subjects to have the pure motor type of imagery who during the masking experiment are able to maintain the correct pitch and volume of tone but are not conscious of any sensation in the larynx. These people assert that while singing during the experiment they suddenly feel well.

The results of Weiss's experiments with persons of the kinesthetic type of imagery confirm the conjectures already named, which I had formed on observations of patients with paralysis of the recurrent nerve. On the basis of Weiss's results certain conclusions which I had previously formulated as a hypothesis may now be drawn. The experiment with the Lombard method can be considered an experiment in interference of the sort used by Baerwald⁶ for the purpose of discovering a possible difference between the so-called actual and potential types of imagery. The actual type is the one which can be observed in oneself if one is told to think silently of short sequences of numbers or short sentences which have just been presented. One subject will see the numbers or sentences before his inner eye. Another will hear the words in his ear. A third will feel slight movements of speech in his mouth even though he tries not to speak. If the same results are consistently, or almost consistently, obtained from many tests using material from many different fields, one can consider the first subject to have imagery of the visual type, the second, of the auditory, and the third, of the kinesthetic, or motor. If, however, there is reason to suspect (as, strictly speaking, there always is) that the type of reaction exhibited by the subject is a result of training, then the experimenter must attempt to interfere with the sense organ in question. In the new experimental setup, i. e., with interference, the subject again observes his reactions to the same material. If he now feels greatly disturbed by the interference, it may be justifiably concluded that the sense organ which responded in the first experiment is the one which most advantageously assists this subject's memory. If, however, another sense organ now distinctly assists him in calling to mind the numbers and sentences, it may be considered that this sense, which immediately substituted for the first, represents the potential type of imagery, which was previously obscured by the actual one. The potential faculty was presumably forced into the background in favor of another, probably on account of training, but possibly also because of other factors. There are undoubtedly numerous occasions on which the impressions on one sense organ are so powerful that they drown out those of another, even though the latter may be congenitally dominant. At such times there is no highly conscious perception in the realm of the latter sense. During singing, for example,

6 Baerwald, R. Zur Psychologie der Vorstellungstypen, Leipzig, 1916

the ear is so preoccupied with the reception of tones that there is no chance for other perceptions to attain a high degree of consciousness unless they are especially intense. It is therefore not surprising that kinesthetic perceptions in the larynx remain practically unnoticed in the background of consciousness until, with the auditory impressions experimentally cut off, the foreground becomes available to them.

The presence of conscious sensations of movement and position in the larynx during singing has thus been demonstrated. These sensations correspond to the fine phonetic processes of tension, stretching and vibration of the vocal cords. It seems, therefore, justifiable to postulate analogous sensations during speech, although experimental evidence to this effect has not yet been obtained. In view of these findings it seems to me possible¹ to throw light on many phenomena which have hitherto not been adequately explained. For example, in numerous cases of unilateral or bilateral paralysis of the recurrent nerve in the abduction position, there is tremendous waste of breath, regardless of the width of the glottis. This phenomenon may, to be sure, be produced partially by reflexes. In support of this supposition one might cite the work of Satta, Ooischi and Utumi,⁷ who recently demonstrated that bilateral section of the recurrent nerve of the dog immediately produced rapid respiration. But the fact that a certain disorder is controlled by reflexes¹ should not deter the investigator from searching for other conditions which may be equally fundamental. It is frequently found that patients with malformations of the mouth and throat exhibit behavior which is inexpedient and undoubtedly conscious. The articulation of patients with cleft palate, for example, deviates from the normal, without exception, to a degree not to be accounted for on a purely anatomic basis. In a lecture delivered in Graz in 1934⁸ I expressed my doubts as to whether a purely mechanical explanation is sufficient to account for the extraordinary waste of breath frequently noted in cases of paralysis of the recurrent nerve with a glottis only 2 or 3 mm wide, or even less. Since normal persons let out breath sparingly, when the glottis is triangular and about 3 mm wide at the base, it seems unlikely that the purely mechanical explanation of the waste of breath in pathologic cases is adequate. If, however, one considers the physiologic sensations in the larynx, already described, and the extremely awkward articulation of patients with cleft palate, one will be led to ascribe the pathologic waste of breath to the confusing influence of the unaccustomed sensations caused by the sudden paralysis of the vocal cords. This seems all the more probable since, as mentioned previously, respiration may return to normal if the paralysis lasts for a long time.

⁷ Satta, Ooischi and Utumi. *Ztschr. f. Oto-, Rhino- u. Laryng.*, vol. 43

⁸ Froschels, E. *Störungen der Atmung bei einigen Erkrankungen des Kehlkopfes*, *Monatschr. f. Ohrenh.* **70** 1104, 1936

CONCLUSION

From all these considerations two main interrelated points emerge

1 With the help of Weiss's experiments, the fact that there are conscious kinesthetic sensations of the so-called finer functions of the vocal cords has been demonstrated

2 From this fact the existence of analogous sensations under abnormal anatomic conditions may be inferred

It is now suitable to inquire what the practical import of these conclusions may be. The answer is threefold

1 A reliable scientific basis has been furnished for the practice of those empiricists who consider the development of specific muscle sensations as one of the main objects in vocal training. Presumably this training is intended to develop sensations not only of the respiratory mechanism, of the mouth and pharynx and of certain extrinsic muscles of the throat, but also of those muscles which control the vibrations of the vocal cords

2 The possible effects of a well founded scientific fact on future research can never be foreseen, aside from its effects, the fact is of importance in itself

3 It is significant to be able to demonstrate that there are conscious factors in certain functions which were hitherto considered as belonging entirely to the problematic realm of the unconscious

LIPOID GRANULOMATOSIS (HAND-SCHULLER-CHRISTIAN DISEASE) INVOLVING THE MIDDLE EAR AND TEMPORAL BONE

HARRY ROSENWASSER, M D

NEW YORK

Lipoid granulomatosis (type Hand-Schuller-Christian disease) occurring in an adult and with diffuse involvement of the middle ear and temporal bone as the sole manifestation of the disease is uncommon. The relative rarity of the condition as evidenced by the paucity of reports in the literature, as well as the extreme difficulty of establishing the diagnosis in this case and the excellent therapeutic result after intensive roentgen therapy, warrant the present report as well as a brief discussion of lipoid granulomatosis.

REPORT OF A CASE

R. H., a woman aged 50, was first observed in the outpatient clinic of the Mount Sinai Hospital on Jan. 6, 1936, with the chief complaint of gradual onset of pain and deafness in the left ear of four years' duration. The pain, which had become continuous, was accompanied by buzzing. Four months prior to admission the patient suffered episodes of transitory facial paralysis and post-auricular pain on the left side. The latter at times radiated to the vertex and was aggravated by chewing. There had been no chills, headaches, convulsions or visual disturbance.

Examination—The patient was a slightly obese woman who did not appear ill. The right ear was normal. In the external auditory meatus of the left ear there was a pulsating seropurulent discharge, which reappeared slowly from beyond a large granuloma that filled the fundus of the auditory canal. There was pre-auricular but no mastoid tenderness. Cochlear and vestibular function were entirely absent in the left ear. The fistula test gave a normal reaction. There was no spontaneous nystagmus. There was, however, spontaneous past pointing mesially with the left hand. The fundi were normal. The tongue deviated to the left, and there was some atrophy of the left half. Laryngeal examination revealed slight limitation of motion of the left vocal cord. There was no evidence of tumor in the nasopharynx.

Roentgenograms of the mastoid processes taken while the patient was attending the outpatient clinic (Jan. 6, 1936) revealed the right mastoid process to be clear. There was diffuse haziness over the entire left mastoid process, the cell outlines

From the Otologic Service of Dr. Jacob L. Maybaum and the Radiotherapy Service of Dr. William Harris, the Mount Sinai Hospital.

were present, except at the tip, where they were more or less obscured. There was moderate sclerosis of the intercellular septums. The patient was admitted to the otologic service of Dr. Friesner, in which fourteen days later a second series of roentgenograms was made. At that time the base plate roentgenograms of the petrous pyramid revealed a large area of destruction in the left petrous bone, extending apparently to the occipital bone. The cause of the lesion could not be determined (fig. 1).

Under the assumption, based both on roentgenograms and on clinical findings, that a neoplastic process involving the temporal bone was present, a thorough search was made for a primary focus. None, however, was found.

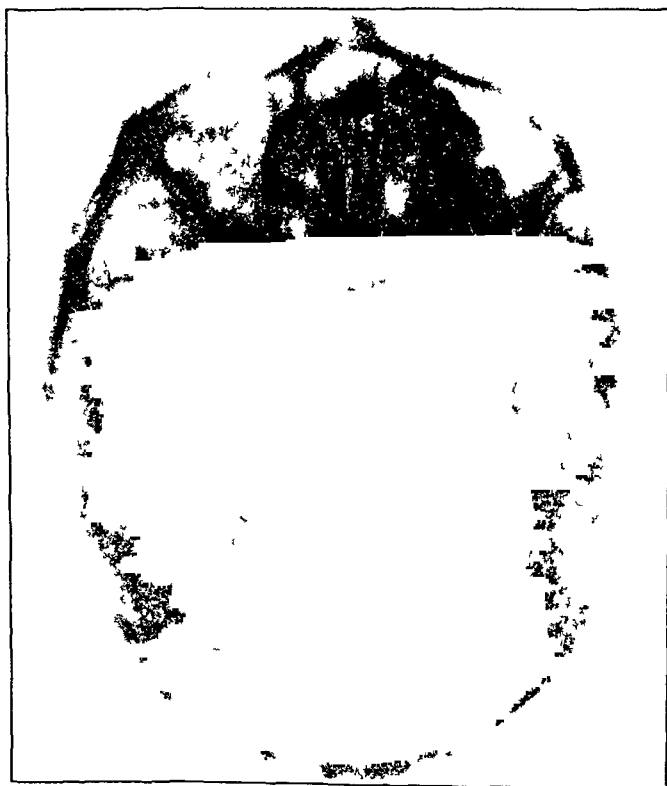


Fig. 1—Base plate roentgenogram of the skull, showing a large area of destruction in the left petrous bone, the lesion extending to the occipital bone.

The Wassermann reaction of the blood was negative. Despite the normal appearance of the nasopharynx, a biopsy was made of material taken from the submucosa but revealed no abnormality. The report on the first biopsy, of material from the granuloma in the external auditory canal, was "vascular granulation tissue."

Operation—A radical mastoidectomy for the purpose of exploration was then performed. The mastoid bone was sclerotic, and there was scanty nonodorous secretion in the initial groove. There was no cholesteatoma. The dura of the middle fossa and the sigmoid sinus then were purposefully exposed, but no

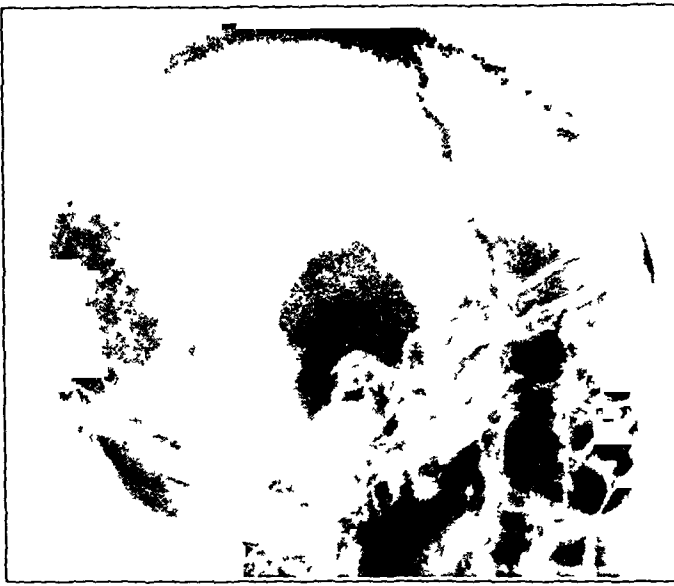


Fig 2—Roentgenogram taken November 1936, approximately ten months post-operatively, indicating the extent of the operative defect necessary to encompass the lesion. The absence of any other manifestations of lipoid granulomatosis in the skull should be noted.

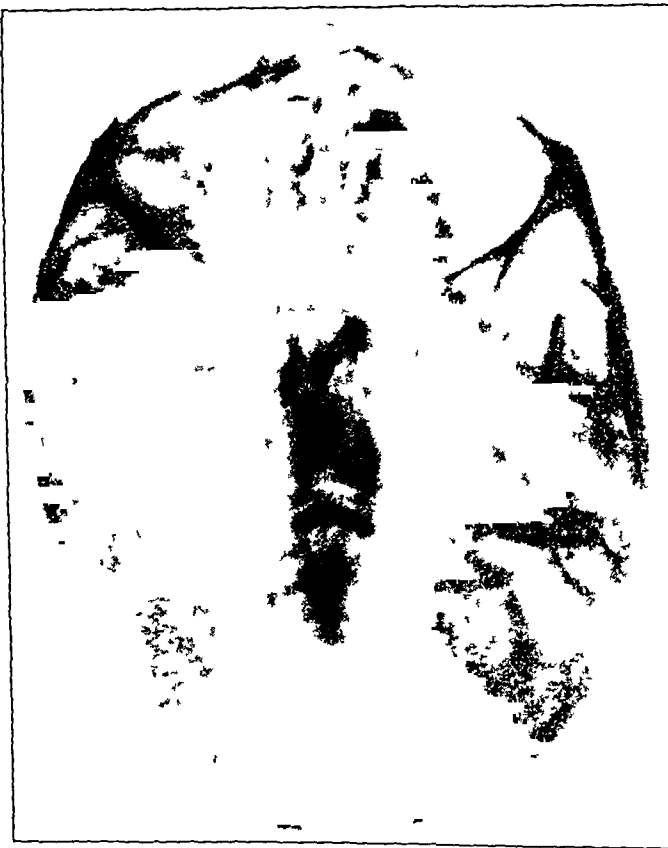


Fig 3—Base plate roentgenogram of the skull, taken Feb 26, 1937, more than one year after operation, revealing deposition of new bone in the defect in the petrous pyramid. The increased calcification in the region of the anterior border of the petrous pyramid should be noted in comparison with figure 1.

abnormality was noted. The inner tympanic wall, which felt soft, bled rather freely when touched. Two specimens were taken from this region. On microscopic examination, one revealed "particles of bone without significant changes." The other specimen, however, revealed "fragments of bone infiltrated with cell nests suggestive of carcinoma simplex."

Postoperative Course—On the assumption that the lesion was a neoplasm, the usual Panse plastic flap operation was not performed. A profuse sanguinous discharge from the middle ear appeared. Shortly after operation, radiation therapy was begun under the direction of Dr. William Harris. After many weeks in the hospital the patient was discharged unimproved and was referred to the

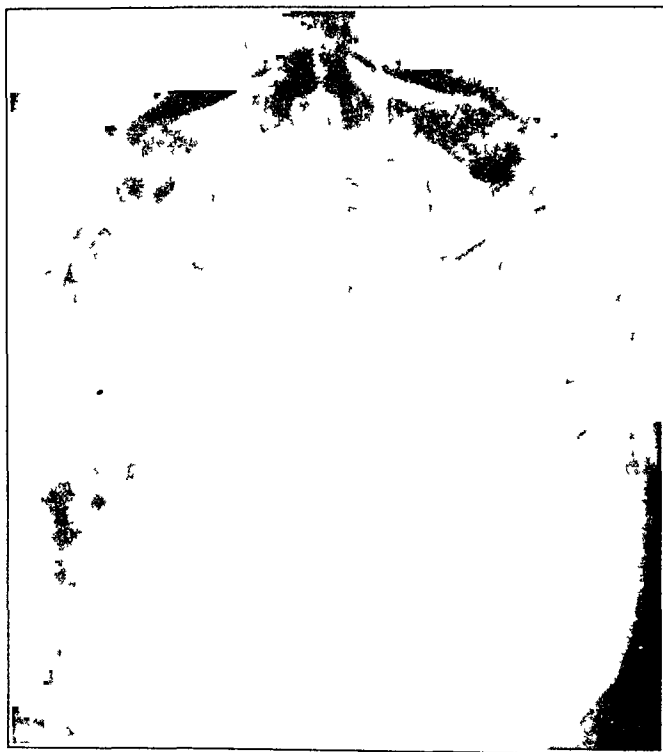


Fig. 4—Base plate roentgenogram of the skull, taken Jan. 19, 1940, more than four years after the original operation, indicating definite evidence of osteogenesis in the defect in the pyramid. The amount of new bone laid down in the pyramid as indicated by the comparative roentgenograms is striking.

radiotherapy department, where she continued to receive treatment. The lesion was treated through two fields—a left preauricular and a left postauricular field, each 10 by 10 cm. A total of 4,000 roentgens (in air) at 180 kilovolts (constant potential) was delivered to each area, in a period of seventy days, with a filtration equivalent to 0.5 mm of copper plus 1 mm of aluminum and a focal skin distance of 40 cm.

Follow-Up—On May 18, 1936 the patient appeared to be in good health and the postauricular wound was healing slowly. In November 1936 she was feeling

well and her headaches had disappeared. Results of blood studies were as follows: Urea nitrogen 8 mg, cholesterol 290 mg, and sugar 85 mg per hundred cubic centimeters. The postauricular wound was healed, and the patient had gained weight and was able to perform her household duties (fig 2). The facial paralysis still was present. In January 1937 the condition was unchanged. In April 1937 the patient appeared to be in good health. The otologic status was unchanged. Roentgenograms made on Feb 26, 1937 revealed evidence of deposition of bone in the large defect in the apex of the petrous pyramid (fig 3). In January 1940 there was no evidence of new lesions either in the skull or elsewhere in the



Fig 5—Low power photomicrograph of a bone marrow space, showing marked cellular reaction of the lipoid granulation tissue

osseous system (chest, vertebral bodies, pelvis or long bones). The general health of the patient was good. She had gained 25 pounds (11.3 Kg) since the previous follow-up examination. The paralysis of the facial nerve had cleared up. The hemiatrophy of the left side of the tongue was unchanged. The right ear was normal. The left external canal was stenosed and dry, and there was no function of the eighth nerve (fig 4). Comparative roentgenograms indicate definite evidence of osteogenesis in the defect.

Comment—Although the clinical course, the roentgenographic findings and the results of pathologic examination of material removed at

operation were consistent with the diagnosis of carcinoma of the middle ear, the course for more than four years after operation was considered so unusual as to warrant a review of the microscopic sections. After studying the sections, Dr Paul Klemperer made the following report:

Reexamination of the sections suggests that the large epithelial cells are macrophages. The cytoplasm is vacuolated and might have contained fat. It is therefore possible that this is a case of lipoid granuloma (figs 5 and 6).

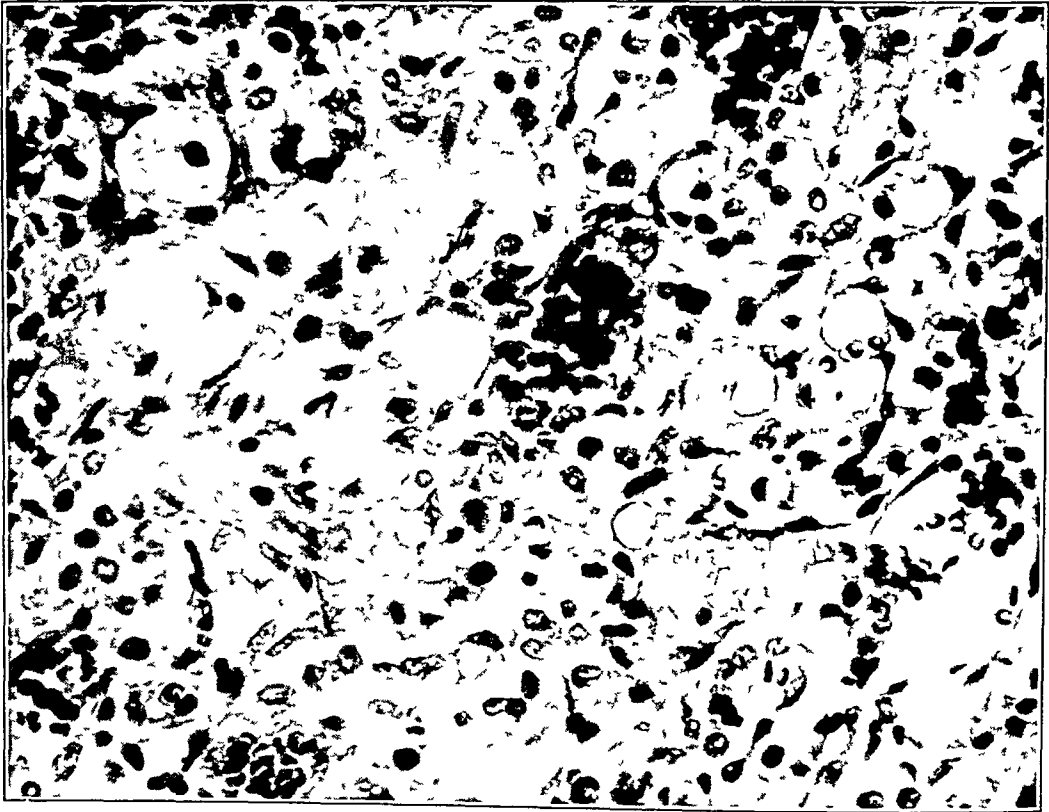


Fig 6—High power photomicrograph of an area in figure 5 which suggests that the large epithelial cells are probably macrophages, the cytoplasm is vacuolated and appears to have contained fat. The diagnosis was lipoid granuloma.

COMMENT

Early observers considered "xanthoma" as usually of inflammatory or toxic origin. Not infrequently, however, its origin was regarded as neoplastic. But the demonstration of lipid substances in the xanthoma cells by Panzer¹ and by Pick and Pinkus² altered these early concepts,

1 Panzer, T. Doppeltbrechende Substanzen aus pathologischen Organen, *Ztschr f physiol Chem* **54** 239-254, 1907.

2 Pinkus, F, and Pick, L. Zur Struktur und Genese der symptomatische Xanthome, *Deutsche med Wchnschr* **34** 1426-1431, 1908.

and lipoid granuloma has since been regarded as an abnormality resulting from a disturbance of lipoid metabolism (Chester,³ Christian,⁴ Chiari,⁵ Ighenti⁶) Rowland⁷ first employed the term "xanthomatosis" and, in his classic paper, presented evidence that Hand-Schuller-Christian disease is but one of several types of disturbance of lipoid metabolism, which also include Gaucher's disease, Niemann-Pick disease, the xanthomas occurring in icterus, diabetes and pregnancy and finally the so-called essential xanthomas. The present discussion concerns itself only with lipoid granulomatosis.

This condition occurs most commonly, although not exclusively, in young children. According to Chester and Kugel,⁸ in 33 of the 50 reported cases the disease occurred in children in the first decade of life. It involves membranous bones, especially those of the skull. It is frequently associated with diabetes insipidus, exophthalmos and gingivitis and to a lesser extent with adiposogenital dystrophy and jaundice. It is not racial or familial, although it seems to be particularly frequent among Jews.

In the fresh state the protoplasm of the typical "xanthoma" cell is filled with small droplets of a lipoid substance which dissolve when treated with ordinary fixing reagents. This leaves a fine areolar network within the protoplasm and gives the cell a vacuolated or foamy appearance (hence the name foam-cell, or *Schaumzelle*). According to Chester and Kugel, the main pathologic features of the lipoid granuloma are (1) the typical foam cell just described, (2) the inflammatory cellular exudate which is a response of the tissues to the lipoid substance, a type of foreign body reaction, and (3) the stage of connective tissue proliferation and eventual fibrosis.

The etiologic factor generally considered common to all members of the xanthoma group is a disturbance of lipoid metabolism. This may be widespread and diffuse, as in Niemann-Pick and Gaucher's disease, or

3 Chester, W. Ueber Lipoidgranulomatose, *Virchows Arch f path Anat* **279** 561-602, 1930.

4 Christian, H. A. Defects in Membranous Bones, Exophthalmos and Diabetes Insipidus, in *Contributions to Medical & Biologic Research Dedicated to Sir William Osler, in Honor of His Seventieth Birthday, July 12, 1919, by His Pupils and Coworkers*, New York, Paul B Hoeber, 1919, vol 1, p 390.

5 Chiari, H. Die generalisierte Xanthomatose von Typus Schuller-Christian, *Ergebn d allg Path u path Anat* **24** 396-450, 1931.

6 Ighenti, W. K. Zur Frage der allgemeinen granulomatosen Xanthomatose, *Virchows Arch f path Anat* **282** 585-612, 1931.

7 Rowland, R. S. Xanthomatosis and the Reticulo-Endothelial System, *Arch Int Med* **42** 611-674 (Nov) 1928.

8 Chester, W., and Kugel, V. H. Lipoid Granulomatosis (Type Hand-Schuller-Christian), *Arch Path* **14** 595-612 (Nov) 1932.

may be localized in granulomatous deposits, as in Hand-Schüller-Christian disease and the cutaneous xanthomas. In the case presented the lesion was a single large one in the temporal bone. The clinical manifestations of the disease depend first on the local effect of the lesion, which may become large, and secondly on the degree of the associated general metabolic disturbance. For example, when the lipoid granuloma is in the orbit, exophthalmos not infrequently results. If the lesion is in the region of the posterior lobe of the pituitary gland, diabetes insipidus is often an early symptom. If, as in the case reported in this paper, the lesion involves the middle ear, the mastoid process and the petrous pyramid, it produces pain, facial paralysis, deafness and headache. The typical lipogranulomatous lesions may occur in persons of any age. According to Rowland, they usually appear as discrete nodular lesions in the slowly evolving adult forms and as more diffuse lesions in the rapidly developing infantile ones. Rapidly developing, fatal, diffuse processes have also been reported as occurring in adults.

Lipoid granulomatosis affects growing children and frequently produces abnormalities of the teeth, ears, trachea, bronchi and vertebral bodies (Berman⁹). As Lederer, Poncher and Fabricant¹⁰ have pointed out, pediatricians, dentists, neurologists and otolaryngologists if aware of the condition are in a position to detect it in cases in which it might otherwise be overlooked. It should be borne in mind that, as stated by Schuller,¹¹ Hofer¹² and Sosman,¹³ there is a marked tendency for spontaneous remission to occur. Improvement has been reported as following the use of a low fat diet. The patient I have reported on did not have hypercholesterolemia and consequently was not placed on a low fat diet. Furthermore, the evidence of the efficacy of this type of treatment is not convincing. Endocrine therapy, including the use of posterior pituitary, thyroid and insulin, and the administration of heliotherapy, irradiated foods, high protein diets and transfusions, also have been employed without demonstrable influence on the osseous defects. On the other hand, according to Sosman,¹³ Lederer, Poncher and Fabricant,¹⁰

9 Berman, W. Xanthomatosis (Lipoid Histiocytosis) of the Spine, *J Mt Sinai Hosp* **5** 419-425 (Nov-Dec) 1938.

10 Lederer, F. L., Poncher, H. G., and Fabricant, N. D. Aural Manifestations of Lipoid Granulomatosis of the Skull, *Arch Otolaryng* **21** 27-40 (Jan) 1935.

11 Schuller, A. Ueber eigenartige Schädeldefekte in Jugendalter, *Fortschr a d Geb d Röntgenstrahlen* **23** 12-18, 1915.

12 Hofer, K. Beitrag zur Xanthomatose der Dura mater und der Schädelknochen, (Schädeldefekte, Exophthalmos Diabetes insipidus, Zwergwuchs), *Klin Wchnschr* **9** 1302-1305 (July 12) 1930.

13 Sosman, M. C. Xanthomatosis, Schuller-Christian Disease, Lipoid Histiocytosis, *J A M A* **98** 110-117 (Jan 9) 1932.

Gilmore,¹⁴ Cignolini,¹⁵ Vampire,¹⁶ Shea¹⁷ and others, the use of roentgen therapy has been attended with uniformly beneficial results in so far as the osseous defects are concerned. Wood¹⁸ told of a case in which progressive bony destruction occurred in three months despite intensive irradiation. In some instances no roentgenographically detectable evidence of osteogenesis in the affected area is noted for many years. Sosman stated that "irradiation presumably kills the already distended and fat-laden histiocytes, liberating the lipoids which are disposed of elsewhere, and allows the individual lesion to heal by the normal course."¹³ Schall¹⁹ expressed the belief that the lesions in these cases heal by nonspecific fibrosis. The important fact to be emphasized is that the lesions of Hand-Schuller-Christian disease, or lipoid granulomatosis, frequently respond to roentgen treatment. From the standpoint of differential diagnosis, it is also important to mention that the osseous defects in Hand-Schuller-Christian disease, or lipoid granulomatosis, may simulate neoplastic processes which involve the skull, i. e., osteogenic sarcoma, lymphosarcoma, chloroma or multiple myeloma.

CONCLUSION

An exceptional result, obtained after a careful follow-up of a case of supposed carcinoma, prompted a review of the histologic sections. Had these slides not been reviewed, it is probable that the case would have been regarded as one of carcinoma, involving the ear and petrous pyramid, cured for four years. The case also demonstrates the difficulty which may be met in establishing a diagnosis, even by the most highly trained pathologists. Furthermore, it indicates an excellent therapeutic result, attributable apparently to the intensive use of the roentgen rays.

14 Gilmore, M. E. Multiple Myeloma Syndrome in a Child, *Texas State J. Med.* **21** 358-362 (Oct.) 1925.

15 Cignolini, P. Effetti locali e generali della radioterapia in un caso di diabete insipido associato ad osteopatia, *Radiol. med.* **16** 16-21 (Jan.) 1929.

16 Vampire, E. Syndrome de Christian, *Rev. sud-am. de med. et de chir.* **1** 459-464 (May) 1930.

17 Shea, J. J. Xanthomatosis (Schuller-Christian Disease). Report of a Case in Which There Was a Radiosensitive Pathologic Growth in the Mastoid, *Arch. Otolaryng.* **28** 1035-1036 (Dec.) 1938.

18 Wood, V. V. Bilateral Xanthomatosis (Lipoidosis) of the Mastoid. Case Report, *Ann. Otol., Rhin. & Laryng.* **46** 991-1008 (Dec.) 1937.

19 Schall, L. A., in discussion on Shea¹⁷

OBJECTIVE TINNITUS AURIUM

REPORT OF A CASE

JOSEPH C DONNELLY, DDS, MD

PHILADELPHIA

Tinnitus aurium is a symptom which is most distressing to a patient and usually is subjective, in that the patient hears the noise. On rare occasions it may be objective, the symptom of which the patient complains being heard by the examiner. An example of this unusual form of tinnitus aurium, the objective type, recently came under my observation, and the problem of diagnosis and management presented unsurmountable difficulties. The purpose of this paper, therefore, is to review these studies in connection with the diagnosis and treatment of objective tinnitus aurium.

TYPES OF OBJECTIVE TINNITUS AURIUM

Objective tinnitus aurium may be of muscular or of vascular origin. The former type is characterized by a curious clicking sound aptly compared by Weil¹ to the noise produced by the snapping together of two finger nails. Low pitched and occurring from 40 to 120 times per minute, it may be heard at a distance of from 1 to 3 feet (30 to 90 cm), and the rhythmic spasm of the muscles at the mouth of the eustachian tube may be visualized with the nasopharyngoscope. This intermittent audible tinnitus may easily be distinguished from the vascular variety, because in the latter the bruit is continuous and is synchronous with the heart beat. The noise in the vascular type has been most frequently compared to the puffing of an engine.

THEORIES OF ORIGIN

Muscular Type—The cause of the muscular type of objective tinnitus is generally attributed to the clonic contractions of the muscles in and around the mouth of the eustachian tube. This cause appears the more likely since the clonic spasm may be viewed with the nasopharyngoscope

From the Department of Otolaryngology of the Hospital of the University of Pennsylvania

Read before the Section on Otolaryngology of the College of Physicians of Philadelphia, Nov 15, 1939

1 Weil, A. A Case of Objective Tinnitus Auri, *Laryngoscope* **14** 202, 1904

Kafke² and others, however, have stated the belief that the snapping sound arises from the violent contractions of either the stapedius or the tensor tympani muscle. In a young man with objective tinnitus aurium recently demonstrated to me by Hunter,³ the rhythmic contractions of the eustachian tube were visible and the snapping bruit with a tempo of 120 times per minute was sufficiently loud to be heard at a distance of over 2 feet (60 cm). An interesting feature in this case, as in the one referred to by Harris⁴ in his discussion of Weil's paper was the voluntary nature of the bruit, the patient being able at times to start or stop the tinnitus at will. In some instances there is an associated movement of the soft palate, as was demonstrated in a case recorded by Jones and Knudson⁵ and in that of a 9 year old girl reported by Friedmann.⁶

Vascular Type—A host of theories have been advanced to explain objective tinnitus aurium of vascular origin. In a consideration of the subject of audible tinnitus aurium it is difficult to confine the study to noises emanating strictly from the ears, since it appears from a review of many records of both the muscular and the vascular type that an entotic bruit invariably has a coexisting head murmur. This paper, however, is concerned primarily with those patients whose initial or chief symptom is a bruit heard in the ears. Hamburger⁷ made no attempt to differentiate an objective tinnitus from a cranial bruit, while Cushing and Bailey⁸ in their monograph used the terms interchangeably.

TRANSIENT BRUIT

Audible tinnitus aurium is usually a chronic symptom, but it is reassuring to know that at times it may be only transient. Hamburger referred to the case of a physician in whom objective tinnitus developed after a severe coughing spell but lasted only six weeks. Another patient observed by Hamburger contracted an audible bruit after swimming, and the murmur ceased spontaneously in six months. The mechanism by which these murmurs were produced and by which their spontaneous disappearance was accomplished could only be surmised. Since each bruit, however, was continuous and was intensified with each systolic

2 Kafke, M. M. Tinnitus Aurium. Etiology, Differential Diagnosis, Treatment and Review of Twenty-Five Cases, *Laryngoscope* **44** 515, 1934.

3 Hunter, R. J. Personal demonstration to the author.

4 Harris, in discussion on Weil.¹

5 Jones, K. H., and Knudson, V. S. Certain Aspects of Tinnitus, Particularly the Treatment, *Laryngoscope* **38** 597, 1928.

6 Friedmann, C. Zur Casuistik der objektiven Ohrgerausche, *Ztschr. f. Ohrenh.* **46** 373, 1904.

7 Hamburger, L. P. Head Murmurs, *Am. J. M. Sc.* **181** 756, 1931.

8 Cushing, H., and Bailey, P. Tumors Arising from the Blood Vessels of the Brain, Springfield, Ill., Charles C. Thomas, Publisher 1928.

thrust, Hamburger assumed that a communication existed between the internal carotid artery and the cavernous sinus. He did not think that violent trauma or a complicating exophthalmos was a necessary accompaniment of such a complication. In support of his belief of the spontaneous obliteration of the communication he told of the case of an arteriovenous fistula recorded by Perier.⁹ A young girl was thrown from a swing and after striking the back of her head became unconscious, the following day a loud cephalic murmur was audible, but without any interference it gradually diminished and disappeared entirely at the end of several weeks.

A transient type of objective aural noises may be an accompaniment of an abscess of the middle ear, as was shown in the case of the hypertensive patient of Bredlau's.¹⁰ The bruit lasted only one week and was attributed by Bredlau to the pulsations of the internal carotid artery.

In pregnancy and during the menopause there are other examples of spontaneous recoveries. Iglauer¹¹ reported the onset of a bruit during the second month of pregnancy which disappeared in the seventh month, while the murmur heard by Moore¹² began in the seventh month and vanished when the uterus was emptied. These observers assumed that the cause was some circulatory disturbance. An endocrine abnormality was considered present in another patient of Iglauer's, who had audible tinnitus during the menopause.

It might be added that even extracranial arteriovenous communications may undergo spontaneous obliteration, as was observed by Reid¹³ in his patient with an arteriovenous fistula of the right subclavian vessels. Operation was refused, but after six months the signs of fistula had disappeared. Reid stated that spontaneous obliteration occurs in six months if it is going to happen at all.

CHRONIC BRUIT

Vascular Anomalies—Persuasive arguments have been proposed to show the relationship between entotic noises and vascular anomalies. Iglauer stated that in view of the close proximity of the jugular fossa,

9 Perier. Bull. et mem. Soc. de chir. de Paris **25** 91, 1909, cited by Hamburger.⁷

10 Bredlau, E. A. Objective Tinnitus Aurium, Arch. Otolaryng. **28** 193 (Aug.) 1938.

11 Iglauer, S. Objective Tinnitus Aurium, Arch. Otolaryng. **18** 145 (Aug.) 1933.

12 Moore, R. L. Entotic Tinnitus Percivable Objectively in Pregnancy. J. A. M. A. **54** 969 (March 19) 1910, cited by Iglauer.¹¹

13 Reid, M. R. Abnormal Arteriovenous Communications, Acquired and Congenital. Treatment of Arteriovenous Communications, Arch. Surg. **11** 237 (Aug.) 1925.

the sigmoid groove and the carotid canal to the middle and the internal ear, it is rather remarkable that audible tinnitus of a vascular origin is not more frequently encountered. Apropos of this anatomic proximity, reference may be made to Ferris Smith's¹⁴ patient, who had a congenital arteriovenous fistula of the jugular bulb and the internal carotid artery. At the age of 24 years this patient had a spontaneous hemorrhage from the right ear and complained of deafness together with a pounding noise in the right side of the head since childhood. It was not stated whether the bruit was objective, but clinical and roentgen examination revealed a total loss of the floor of the tympanum and the external auditory canal, through which could be seen a pulsating pinkish blue mass.

The patient reported on by Moos¹⁵ suffered from severe subjective tinnitus and auditory hallucinations for many years, at necropsy Moos found a tremendously enlarged jugular bulb, which led him to believe that this anomaly was sufficient to explain the severe tinnitus. Bagley's¹⁶ case study, dealing with a young woman who had a cranial bruit for four years and died at the age of 20, was more convincing, necropsy revealed dilated venous channels, and their tributaries lay in deep depressions in the skull. This picture was not unlike that recorded by Courville¹⁷ in a discussion of Viole's¹⁸ paper, when he referred to the autopsy observations associated with a widespread dilatation of the dual sinuses in a patient who had suffered from a loud murmur over most of the cranial vault.

Clinically, there is the unique report of Hoover's¹⁹ patient, who had an audible tinnitus in the left ear which could be abolished by pressure over the cervical vessels. Hoover decided to ligate the carotid artery, but to his surprise at operation compression of the artery only raised the pitch of the bruit while pressure on the internal jugular vein obliterated it. Ligation of the vein was performed, and the patient has remained well without any untoward symptoms for the past ten years.²⁰ Hoover expressed the opinion that a unilateral bruit which can be controlled by pressure over the internal jugular vein is due to some abnormal vibration of the vein and may be controlled by ligation. Iglauer

14 Smith, F. Congenital Arteriovenous Fistula in the Tympanum, *Arch Otolaryng* **10** 32 (July) 1929.

15 Moos. Ueber einen Fall von Erweiterung des Bulbus venae jugularis, *Arch f Augen- u Ohrenh* **4** 174, 1874, cited by Weil.¹

16 Bagley, C, Jr. Blood in the Cerebrospinal Fluid, *Arch Surg* **17** 18 (July) 1928, cited by Iglauer.¹¹

17 Courville, in discussion on Viole.¹⁸

18 Viole, P. Objective and Subjective Tinnitus of Vascular Origin, *Tr Am Laryng, Rhin & Otol Soc* **41** 526, 1935.

19 Hoover, W B. Left Carotid Jugular Arteriovenous Communication, *S Clin North America* **9** 1453, 1929.

20 Hoover, W B. Personal communication to the author.

noted that in his 4 cases and in 4 others gathered from the literature a unilateral audible tinnitus could be stopped by pressure over the internal jugular vein and markedly influenced by torsion of the patient's head about the vertical axis. When the head was turned toward the side of the bruit the intensity of the noise was perceptibly decreased, while if the head was turned toward the unaffected side the murmur was materially increased. Iglaue¹ assumed that the rotation of the head had some effect on the circulation in the jugular vein and bulb, since one could hardly expect such a torsion of the neck to produce much influence on the more rigid carotid artery. Like Moos, Iglaue stated the belief that if a unilateral bruit can be stopped by pressure on the internal jugular vein and perceptibility influenced by torsion of the neck, the lesion may be attributed to some anomalous condition of the venous channels on the affected side, and he suggested ligation of the internal jugular vein in cases in which the symptoms are intractable.

Intracranial Aneurysm When there is occasion to examine a patient suffering from objective tinnitus aurium, so commonly associated with a concomitant cranial bruit, it appears that the possibility of an intracranial aneurysm is immediately considered. The erroneous belief that such a lesion is the cause of the noise has been commented on by Beadles,²¹ who in a study of 555 cases of proved intracranial aneurysm disclosed the rather startling fact that only 2 patients had a murmur which could be heard during life. The aneurysms in these 2 patients were demonstrated at necropsy as intracranial aneurysms of the vertebral and the internal carotid artery respectively. Cushing and Bailey also expressed agreement as to the rarity of a bruit associated with this condition.

Extracranial Aneurysm On the other hand, extracranial aneurysms are not infrequently found producing objectively audible ear noises. In the case reported by Hamburger the temporal artery was involved, and in Kuttner's²² case the bruit originated in the occipital artery. Both bruits were abolished by ligation of the affected vessels.

Traumatic Arteriovenous Aneurysm A well recognized cause of audible tinnitus aurium with an accompanying cranial murmur may be found in cases of arteriovenous aneurysm of traumatic nature in which the clinical findings point toward a communication between the internal carotid artery and the cavernous sinus. Through the courtesy of the late Dr. Charles F. Nassau I have had the privilege of presenting before the Section on Otolaryngology of the College of Physicians of Philadelphia a patient with such a syndrome. The terrific noise began in

21 Beadles, C. F. Aneurysms of the Larger Cerebral Arteries, *Brain* **30** 285, 1907.

22 Kuttner. *Zentralbl. f. Chir.* **39** 1162 1912, cited by Hamburger.

this patient's right ear immediately after a fall, and although heard best in the ear the bruit was audible over the entire head. Two months later the man returned to the hospital because of an unbearable headache and a progressively increasing exophthalmos. After ligation of the common carotid artery by Dr. Nassau the headache disappeared and the exophthalmos decreased. The patient states, however, that the day following operation the bruit was heard in the other ear and has remained bilateral to the present. It has a smooth, blowing quality unlike the rather harsh, scraping noise of the spontaneous tinnitus in the case to be reported presently. But in the main the characteristics are similar, in that the bruit is continuous and is reinforced with each systolic contraction of the heart.

In Callander's study²³ of arteriovenous fistulas, mention is made of the mechanics of the murmur. Broca²⁴ and Henry²⁵ said they thought the bruit was caused by the vibration of the communication when its borders were set in motion by the continuous passage of arterial blood, while Burckhardt²⁶ ascribed it to the clashing of the venous and the arterial column of blood flowing in opposite directions.

Arteriovenous Angioma. Under the broad heading of vascular anomalies may be considered the angiomatous malformations which not uncommonly have a coexisting objective tinnitus or cranial bruit. The excellent monograph of Cushing and Bailey⁸ on blood vessel tumors of the brain has been a beacon of light in my study, and from their text I must quote freely. These vascular malformations are referred to as arterial or arteriovenous angiomas and are congenital, having from the beginning arterial and venous components. Although these abnormal vessels may be present from birth, the establishment of a communication between the anomalous arteries and veins may not occur until adult life. Dandy²⁷ remarked that the late appearance of symptoms is one of the most surprising features of this lesion, in his experience 44 per cent of the patients did not have their first symptom until after the age of 30 years, and in 30 per cent symptoms began after the fortieth year.

The majority of arteriovenous angiomas have been found on the surface of the brain, as shown in the figure, and appear to have a pre-

23 Callander, C. L. Study of Arterio-Venous Fistula with an Analysis of Four Hundred and Forty-Seven Cases, *Johns Hopkins Hosp. Rep.* **19** 260, 1920.

24 Broca, P. Aneurysme arterio-veineux du pli du coude, *Bull. Soc. de chir. de Paris* **4** 392, 1863, cited by Callander²³.

25 Henry, A. A. Considerations sur l'aneurysme arterioso-veineux, Thesis, Paris, no. 70, 1856.

26 Burckhardt, C. Ueber den Varix aneurysmaticus, *Arch. f. physiol. Heilk.* **2** 114, 1843, cited by Callander²³.

27 Dandy, W. E. Arteriovenous Aneurysm of the Brain, *Arch. Surg.* **17** 190 (Aug.) 1928.

dilection for the temporal lobe²⁸ Then gross appearance was described by Cushing and Bailey as follows

The central portion of the lesion is a fairly well circumscribed vascular area, composed of manifold, partly thinned and partly thickened vascular trunks forming an inextricable coil of dilated and sinuous vessels of varied caliber through which the arterial blood passes from enlarged entering arteries directly into one or more dilated veins of exit usually with the production of an audible bruit

In only 1 patient of their series of 9 presumed or proved to have aneurysmal angioma did they fail to detect a cranial bruit either before or after operation In 1 patient the bruit (audible tinnitus aurium) was the initial symptom, and the lesion was found in the temporal lobe The same is true of an occasional case recorded in the literature, such as that briefly described by Maklakow²⁹ Reinhoff's³⁰ patient, a woman of



Photograph of an arteriovenous angioma exposed at operation (Courtesy of Dr R A Groff, who made the photograph and gave permission for its use)

59 years, had audible tinnitus aurium, which she compared to the puffing of an engine, and the bruit, heard downward into the suboccipital region, could be obliterated by light pressure over the carotid artery It was noted that the noise could be made to disappear by light pressure at so many points that no single vessel could be held responsible for the murmur At that time Dandy ventured the opinion that the condition was angiomatous and involved the occipital arteries and veins The final

28 Groff, R A Personal communication to the author

29 Maklakow, A Un cas de telangiectasie du cervelet, *Ann d'ocul* **151** 252, 1914, cited by Cushing and Bailey⁸

30 Reinhoff, W F, Jr Congenital Arterio-Venous Fistula An Embryological Study with the Report of a Case, *Johns Hopkins Hosp Bull* **35** 271, 1924

outcome is not known. Recently Sears³¹ reported the necropsy observations associated with a cerebral aneurysmal angioma in a man of 44 years who had an audible cranial bruit. Like Hamburger, Sears described the murmur as being continuous, with a systolic intensification.

Tumor of the Brain Cerebral tumors of the vascular type, such as meningiomas and gliomas, rarely produce an audible bruit. The symptoms are generally manifested in the later years of life, and roentgen evidence is usually found in the skull.

Systemic Diseases The cranial bruit associated with the systemic diseases, e. g. valvular lesions of the heart, exophthalmic goiter, arteriosclerosis and anemia, is usually only objective, not being audible to the patient, as the experience of Hamburger testifies. In a woman of 60 years suffering from exophthalmic goiter a short blowing systolic murmur could be heard throughout the head, while in a boy of 6 years a loud cardiac systolic murmur, the aftermath of rheumatic disease, was transmitted to the back and audible all over the head. Neither of these loud murmurs was heard by the patient.

REPORT OF CASE

At the time studies were conducted on this patient the subjective and objective bruit was confined to the left ear. Two months later, after leaving the hospital, the patient noticed in her right ear a similar noise, although much less pronounced. Today the murmur may be heard bilaterally, but faint and inconstant in the newly affected ear.

P. G., a married woman aged 31 years, was first examined in July 1938 because of a noise in the left ear of twelve years' duration. The course of events at the onset is rather vague, but she was apparently in her usual good health and had not been troubled with any disease of the upper respiratory tract. There was no history of epilepsy, aural infection or a fall which might have led to some intracranial injury. The noise, which she compared to the buzzing of a locust, had been almost constant during the year preceding her admission, and while she was annoyed during the day she was particularly distressed at night in trying to fall asleep. The pitch of the tinnitus varied, and at times the noise appeared to stop for a minute or two only to recur with its usual intensity. The patient's husband volunteered that he could hear the noise and that it was first heard by him after their marriage six years before, which was six years after the subjective symptoms were first complained of by the patient. Her husband was able to corroborate her statement that the murmur was less audible when she was resting on her left side, as a matter of fact, he encouraged her lying in this position because at times he was a little disturbed by the constant noise.

On several occasions during the past two years the patient had suffered from a left-sided temporoparietal headache, which was often accompanied by such tenderness over that area that combing her hair was painful. Furthermore, during the past

³¹ Sears, W. G. Head Noises and Cranial Bruits, *Guy's Hosp. Rep.* 88:308, 1938.

two years she felt a throbbing sensation in the left temporoparietal area, accompanied by frequent dizzy spells but no nausea. The dizziness appeared to be precipitated by certain movements of the head, e. g., those occurring when she stooped over or rose from a recumbent position. Recently she had experienced peculiar circulatory episodes characterized by flushing of the face and coldness of the upper and lower extremities. With the onset of the latter symptoms the noise in her ear was distinctly exaggerated.

Five years before admission she completed a full term pregnancy with no particular alteration of her symptoms, and it does not appear that the menstrual period bears any perceptible relation.

The first examination revealed an extremely apprehensive patient, so apprehensive that the study was necessarily hurried. The nasal passages were free of secretions, in fact there was no evidence of nasal or sinusal abnormality. The larynx and throat were normal. Both tympanic membranes were intact, and there was only a slight diminution of the light reflex. Use of a Siegle otoscope revealed normal motility of the drum heads. No spontaneous movement of the drum was noted on the left, or affected, side. The hearing was within normal limits, with the acuity even greater in the left ear than in the right. The Weber test showed no lateralization, and the reaction to the Rinne test was positive in both ears. The eustachian tubes were patulous, and inflation had no effect on the tinnitus. The bruit in the left ear was a harsh scraping noise synchronous with the heart beat and easily heard with the auscultation tube, although even more pronounced when the examiner placed his ear in contact with that of the patient. This murmur was readily stopped, both to the patient and to the examiner, by light pressure over the cervical vessels adjacent to the anterior border of the sternocleidomastoid muscle.

Later examinations demonstrated that the noises were distinctly obliterated both subjectively and objectively by light pressure over the course of the internal jugular vein. (It may be remarked here that the bruit is evanescent and that during the examination it momentarily disappeared. This spontaneous cessation, however, was not of sufficient duration and frequency to interfere with the accuracy of the clinical tests.) Movements of the head had a perceptible influence, and when the head was turned completely to the left side the bruit faded away. With the head turned to the right the murmur became louder both to the patient and to the examiner. This torsion of the head on the vertical axis was repeated on several examinations, and the findings, while occasionally at variance, were for the most part consistently those just described. No cervical adenopathy was noted. The thyroid gland was of normal size, and no pulsations were discernible in the neck.

Sedatives given over a period of a few weeks were ineffectual, and on Sept. 13, 1938 the patient was admitted for a complete study to the service of Dr. George M. Coates at the Hospital of the University of Pennsylvania.

The patient showed slight secondary anemia, and the blood pressure was 115 systolic and 80 diastolic. The findings were practically the same in both arms. Reactions to the Kolmer and the Kahn test were negative. The basal metabolic rate was -7 . There was nothing in the history or the physical examination to warrant an endocrine study. No cardiac murmurs or evidence of premature arteriosclerosis was found.

In view of a slight ptosis of the right upper eyelid and a slightly diminished prominence of the right nasolabial fold, the question of involvement of cranial nerves was given immediate consideration. Dr. William Cadawaller was consulted and gave the following report: "The movements of the right side of the

face are well performed and although not so well performed as on the left I believe this is of no consequence. It does not indicate a seventh nerve palsy. The right eyeball appears more prominent than the left, which is probably the reason for the apparent ptosis of the upper lid. I believe that the right lid does not show a true ptosis but that the condition is a result of a mechanical difficulty without involvement of the third nerve."

An ophthalmic examination by Dr W E Fry revealed the muscle balance to be within normal limits and the visual fields full. The right fissure was narrower than the left. The pupils were equal and reacted promptly to direct and indirect light. The finger tension was normal. No pulsations were noted from either globe. The media of the right eye were clear, and the disk was well defined and of good color. There were no changes in the macula, vessels, choroid or retina. The findings in the left eye were similar to those in the right. The diagnosis at this time was ptosis of the right upper eyelid. There was no evidence of neuritis or engorgement of the vessels of either eye.

The report on an examination made three months later was as follows. The right fissure was narrower than the left. There was a fine rapid nystagmus on lateral gaze in both eyes. Rotations were full to inspection. The right pupil at times seemed larger than the left, reactions were normal in both pupils. No diplopia was observed with light and red glass. There was no evidence of beginning choking or neuritis. No changes appeared in the macula, choroid or retina. There were no intraocular changes indicative of increased intracranial pressure.

After making a neurologic examination, Dr A M Ornstein said he thought that the condition proceeded from an anomalously placed artery in the middle ear but that the bruit was not of the aneurysmal type. Results of a neurosurgical study by Dr Robert A Groff were negative, except that the palpebral fissure was seen to be narrower on the right side than on the left. The motor, the sensory and the cerebellar system were normal. Dr Groff observed that the bruit was audible in the left temporoparietal area and the right parietal area and agreed with me that the murmur could be stopped by light pressure over the internal jugular vein. He compared the objective tinnitus to the noise produced by the grating of teeth and concurred with Dr Ornstein that the bruit was unlike that heard in association with an aneurysm.

My co-workers and I were particularly concerned with a roentgen examination of the skull in the regions of the jugular fossa, the sigmoid groove and the carotid canal, because it was thought that some anomaly of the large cranial vessels might be demonstrated. Several efforts by Dr E P Pendergrass and Dr George W Chamberlain failed to show any anatomic abnormality or evidence of intracranial mass lesion. The study also revealed no evidence of increased vascularity of the skull.

With the general study completed, our efforts were centered more on the examination of the ear. Dr Julius Winston reported that the vestibular mechanisms functioned within normal limits. An audiometric test pointed toward a slight impairment of hearing, 17 per cent, in the left ear and 19 per cent in the right. With the audiometer it was possible to match the pitch of the tinnitus at approximately 128 double vibrations per second. On several subsequent examinations it was noted that the bruit could be easily heard in the left temporoparietal and the left mastoid area and that occasionally it was even radiated to the right temporo-parietal area.

Comment—A resume of the factors which influenced the tinnitus in the left ear is as follows

1 The most striking clinical demonstration was the immediate cessation of the noise both subjectively and objectively when light pressure was applied to the internal jugular vein

2 Certain rotary movements of the head definitely altered the bruit

3 Exercise immediately exaggerated the rate and intensity of the murmur both to the patient and to the examiner

4 Change of posture from a sitting to a reclining position increased intensity both subjectively and objectively

5 Closure of the auditory canal magnified immediately the noise heard by the patient

6 On deep inspiration the bruit was more audible objectively

7 The use of drugs which Dr O V Batson suggested as an aid in corroborating the vascular origin of the tinnitus had the following effects When the patient inhaled ammonia fumes the blood pressure as well as the rate and intensity of the tinnitus increased When amyl nitrite was inhaled there was a momentary increase in the blood pressure and in the intensity of the bruit, but as the blood pressure dropped the murmur was distinctly less audible both to the patient and to the examiner Under the stimulus of the ammonia gas the continuous character of the bruit was exaggerated and the systolic component intensified

COMMENT

The mechanism in the production of this audible tinnitus is not known, and one can only conjecture the cause It is felt, however, that the greater number of suggested causes, e g systemic diseases, tumor of the brain and intracranial or extracranial aneurysm, have been ruled out The clinical findings do warrant a further consideration of the possibility that some type of vascular anomaly is present

The conspicuous venous element of the bruit is strikingly demonstrated when by light pressure over the internal jugular vein the noise can be immediately obliterated Furthermore, when the patient's head is turned toward the affected ear the bruit is dampened, and if the head is moved in the opposite direction the murmur is increased In view of this demonstration Iglauer's hypothesis seems tenable, for the torsion of the head on a vertical axis may be construed as having a perceptible influence on the circulation within the internal jugular vein rather than any effect on the more rigid carotid artery These findings, in the absence of any recognizable intracranial disease, might lead one to believe with Iglauer and Hoover that in cases of a unilateral entotic murmur of an objective nature the pathogenesis might be explained on

the basis of some anomaly in the jugular bulb or vein and could be controlled by ligation of the vein. If, however, one holds to the belief that the bruit arises from a purely venous anomaly, one would be at a loss to explain the pronounced systolic intensification, on the other hand, if the hypothesis of a simple arterial malformation is accepted, it is difficult to understand the demonstrable venous component.

In our quandary my associates and I, prompted by Hoover's success in obliterating an audible bruit by ligation of the internal jugular vein suggested this procedure but did not urge it. At first the patient was receptive, but later she refused operation. After two months when the bruit became subjectively and objectively present in the other ear, it was felt that the theory of a unilateral venous anomaly was less tenable. It may be remarked that had surgical intervention been carried out, the operation would have been, to say the least, improperly evaluated.

To explain the existence of objective tinnitus aurium, I am calling attention to the possible presence of the unusual intracranial abnormality, arteriovenous angioma. The bruit in my patient, which is continuous and is intensified with each systole of the heart, is typical of the murmur which Hamburger associated with arteriovenous angiomas and which Sears described as occurring in his patient in whom an arteriovenous angioma was observed at necropsy. In Reinhoff's case, factors similar to those in my own were observed, e. g. the bruit could be accentuated by occluding the auditory canal or having the patient assume the recumbent posture. Furthermore he stated that light pressure over the carotid artery obliterated the murmur, but it appears to me that light pressure would hardly have any perceptible influence on the walls of a carotid artery, especially in a woman of 59 years. Hoover was misled in this direction when he thought the bruit of his patient could be controlled by application of pressure over the carotid artery, only to learn at operation that it was the jugular vein that was being compressed. It is not unlikely therefore that in Reinhoff's case, for which Dandy ventured the diagnosis of an arteriovenous angioma, the bruit was obliterated by pressure over the venous structures, as in my case, rather than over the more rigid carotid artery.

An intracranial bruit has been an outstanding feature in 8 out of 9 cases reported by Cushing and Bailey, in which a presumptive or proved diagnosis of arterial angioma was made and it must be concluded from their studies that when the bruit is coupled with signs of increased extracranial vascularity the combination of symptoms is overwhelmingly in favor of an arteriovenous angioma. While my associates and I have been unable to find evidence of extracranial circulatory disturbance, it is pertinent that our patient has symptoms distinctly referable to her scalp and frequently is troubled with a tenderness that at times makes it painful to comb her hair. In this temporoparietal area she experiences

the throbbing sensations, and it is here that the bruit may be so easily heard. The symptoms and clinical findings point toward a vascular lesion in the region of the temporal lobe.

Some authors, e. g. Eimer and Mehlhose,³² have said that they regard epileptiform seizures as one of the essential manifestations of a cerebral angioma, but our patient, as well as 4 of the 9 patients reported on by Cushing and Bailey, has been exempted from epileptiform attacks. The patient I have reported on revealed no signs of increased intracranial tension, and the results of the roentgen examination were negative. These findings are not surprising, for in 2 of Dandy's patients with a localized erosion of the inner table of the skull, shown at operation, the roentgen examination failed to disclose the lesion, and of his series of 8 patients in only 2 were changes in the eyegrounds revealed.

SUMMARY

The case of a patient with objective tinnitus aurium of the vascular type presumably arising from an arteriovenous angioma is presented.

The different causes of objective tinnitus aurium are discussed.

Brief mention is made of the various forms of treatment.

In cases of chronic tinnitus aurium, auscultation might reveal more instances of objective tinnitus.

³² Eimer, K., and Mehlhose, K. Das klinische Bild des zerebralen Angioma racemosum arteriale, München med. Wchnschr. **74** 836, 1927, cited by Cushing and Bailey.⁸

ANGIONEUROTIC EDEMA OF THE LARYNX DUE TO SENSITIVITY TO CHICLE

REPORT OF A CASE

DAVID I FRANK, M D

NEW YORK

Angioneurotic edema has been described by Jackson¹ as a disease characterized by transient circumscribed edematous swellings on mucosal or epidermal surfaces or on both. The larynx alone may be involved, but more commonly there are associated lesions in the gastrointestinal tract, esophagus, mouth, tongue, pharynx, lips, eyelids, skin or genitalia.

There are many causes of edema of the larynx, for example, acute infections of the pharynx and the larynx, disorders following ingestion of hot liquids or foods, inhalation of powerful chemicals, nephritic and cardiac conditions, prolonged use of iodides, foreign bodies in the piriform sinuses, bronchi or upper part of the esophagus, tuberculosis, syphilis, leprosy and neoplasms of the larynx, and wounds of the larynx. The distinction between the angioneurotic type of laryngeal edema and the conditions just named presents little difficulty. The typical picture of angioneurotic laryngeal edema is that of a patient suddenly seized with a tickling cough, a lumpy feeling in the throat, difficulty in swallowing and dyspnea of varying degrees, with or without hoarseness, together with angioneurotic manifestations in other regions, such as the skin, nose and eyes and possibly the gastrointestinal tract. A family history of similar or other manifestations of allergy is frequently present. Osler² reported the occurrence of angioneurotic edema throughout five generations in one family. Even in the absence of such a history or of associated findings such as those mentioned, acute edema of sudden onset accompanied by the symptoms described is usually of the angioneurotic type. The edema, as observed in mirror laryngoscopic examination, differs from the inflammatory and nephritic edema, which convey an impression of watery softness like that of an edematous polyp. Angioneurotic edema does not look as if a puncture would liberate water, it appears firmer.

1 Jackson, C, and Coates, G M. The Nose, Throat and Ear and Their Diseases, Philadelphia, W B Saunders Company, 1929, p 833

2 Osler, W. Hereditary Angioneurotic Edema, Am J M Sc 95 362, 1888

Allergy is not always responsible for angioneurotic edema whether in the larynx or elsewhere. Fink and Gay,³ in a critical review of 170 cases of urticaria and angioneurotic edema, divided the patients into the following five groups on the basis of etiologic factors: (1) those with urticaria associated with foci of infection, 30 per cent, (2) the allergic group, 22 per cent, (3) the psychogenic group, 18 per cent, (4) the endocrine group, 5 per cent, and (5) those whose condition was of undetermined cause, 25 per cent.

They found that in the allergic group avoidance of the specific offender relieved all the patients of their symptoms. Of those patients with foci of infection, they reported that, after the removal of foci, 74 per cent were free of symptoms. Those in the endocrine and psychogenic groups were little relieved after institution of endocrine or psychic therapy.

Angioneurotic edema when it affects the larynx becomes a serious condition. The dyspnea with impending asphyxia that occurs when the edema is pronounced demands careful watching and preparation for a tracheotomy. If the glottic space is greatly narrowed and if local measures have failed, hospitalization is imperative, so that the laryngologist can proceed with a tracheotomy within a few minutes should he find it necessary. Jackson has repeatedly preached early tracheotomies. He has published statistics that show that 33 per cent of the patients who have died from angioneurotic edema of the larynx have died because of the want of prompt tracheotomy.

REPORT OF A CASE

A man aged 22 years was brought to my office on Sept. 13, 1939 by a fellow worker. The following history was elicited. About 1 o'clock of that day, while engaged at his usual duties as a package-wrapping clerk in a department store, he was offered by a customer a piece of chewing gum which he accepted and began to chew. Five minutes later he had a lumpy choking feeling in his throat together with a sensation of dryness and nausea which prompted him to expel the gum immediately. He then went to lunch despite the discomfort, and while waiting for a sandwich and coffee he felt his face becoming warm and his eyes beginning to tear. His face and extremities began to swell, and he felt itchy. He managed to eat the sandwich, although he experienced moderate difficulty in swallowing. The choking sensation in his throat became more annoying, and he also began to have much watery nasal discharge associated with sneezing. He left the restaurant and reported his discomfort to his employer, who directed him to my office, where he arrived at 2 p. m., being transported by cab. He was nauseated on arrival and soon vomited. He felt faint and had to be revived while sitting in the treatment chair.

³ Fink, A., and Gay, L. Critical Review of One Hundred and Seventy Cases of Urticaria and Angioneurotic Edema Followed for a Period of From Two to Ten Years, *J. Allergy* 5 615, 1934.

Examination on Admission—There was unquestionable evidence of a constitutional allergic reaction as manifested by generalized giant urticaria, suffusion of the conjunctiva with lacrimation, coryza, syncope and vomiting. Intranasal examination revealed the typical allergic, waterlogged, turgescient mucous membrane of the turbinates and the septum, with much watery secretion in both nasal chambers. The larynx presented on mirror examination a moderate to marked edema of both arytenoids and aryepiglottic folds as well as slight edema of the epiglottis. The anterior half of each true cord was seen but was not involved. The glottic space was definitely narrowed, but not sufficiently to cause any dyspnea.

Treatment and Course—The patient was given 10 minims (0.61 cc) of solution of epinephrine hydrochloride subcutaneously, which noticeably relieved him of the generalized edema and urticaria within ten minutes after injection. He manifested a sensitivity to epinephrine by reacting with generalized tremors and tachycardia, a reaction which was controlled by hypodermic injection of $\frac{1}{6}$ grain (0.01 Gm) of morphine sulfate. He was then put to bed and observed until 4:30 p. m. Being concerned particularly with the laryngeal edema, I examined the larynx at fifteen minute intervals and was able to observe a progressive diminution in the edema. Examination of the larynx at 3 p. m., one hour after the initial examination, revealed an entirely normal larynx. I permitted the patient to leave for home at 4:30 p. m., at which time examination showed little evidence of the generalized edema and giant urticaria. The conjunctival suffusion persisted, as did the nasal edema. The patient was given capsules of ephedrine and amytal and was directed to take a capsule every three hours until bedtime.

He returned the next day at noon, when recovery was complete. A further history was then obtained, and he was subjected to a thorough allergic work-up. Results of examination and of questioning follow.

Past History—The patient did not recall ever having had any previous attacks of urticaria. For the past six or seven summers he had had attacks which he termed "prickly heat rashes." He catches colds frequently, sneezes occasionally and has frequent supraorbital headaches. He has observed that chewing gum induces a dry feeling in his mouth, with marked nausea and a desire to vomit. On that account, he rarely indulges in chewing gum, only on the insistence of the customer did he do so on this occasion. He has experienced a similar disagreeable sensation when eating apples or pears, but it has not been as pronounced. His tonsils were removed during childhood. There is no evidence of allergy in his immediate family, although there is a possibility of asthma in a first cousin.

Examination of Ears, Nose and Throat—The nasal septum was deviated to the right, and there was obstruction to ventilation and drainage. Moderate hypertrophy of all turbinate bones was noted. The mucous membrane was diffusely red. There was no evidence of the turgescence of the mucous membrane seen in allergy. Mucopus (1 plus) was present on both floors and in the middle meatus on the left side. The tonsils had been removed. The pharynx was red and granular, and there was mucopus (1 plus) postnasally. Transillumination of the sinuses revealed dullness of both antrums. Roentgen examination showed clouding of both antrums and of both frontal sinuses. The larynx was normal. There was moderate retraction of both ear drums.

Intradermal Tests—There were marked reactions to the following inhalants and foods: orris, tobacco, bakery sweeps, dust, various trees, plantain, rice, pork, chocolate, corn, orange, apple, pear and coconut.

I obtained some chicle extract from Dr. A. I. Kleinman, of Brooklyn, who had reported 2 cases of sensitivity to chicle in the *Journal of the American Medical*

Association,⁴ which, it appears, are the only cases of chicle allergy so far reported in the literature. The concentration of the extract was 0.015 mg of nitrogen per cubic centimeter of extract, and from this dilutions of 0.0015 mg and 0.00015 mg were made. Intradermal tests with the strongest dilutions elicited a local reaction with pseudopods which almost covered the entire tested surface of the arm. About five minutes after the introduction of the extract, the patient became restless and felt itchy, his eyes became red and his nose was stuffed. I gave him 8 minims (0.49 cc) of solution of epinephrine hydrochloride and applied tourniquets above and below the tested site to prevent further absorption and more pronounced constitutional symptoms. Tests with the weaker solutions gave marked local reactions but no constitutional symptoms.

Serum of the patient was then prepared for the passive transfer test, and 5 normal subjects were used. All of these persons received intradermal tests with chicle extract, and all failed to give a positive cutaneous reaction. One of the 5 gave a definite positive reaction to the transfer test on the area of sensitized skin with the 0.015 mg extract. The others failed to give a positive reaction to the transfer test.

I had been eager to observe the reaction of my patient by having him chew gum again (clinical trial), but he refused, declaring that he had divorced himself from chewing gum forever.

To eliminate the possibility that ingredients other than chicle might have been responsible for the allergic reaction, I wrote to the manufacturers, requesting the contents of the gum used by my patient. They informed me that the chewing gum contains the following ingredients: chicle gum base, sugar, corn syrup, sweetened condensed milk, molasses, corn starch and a flavor of clove oil and cinnamon oil. Intradermal tests with corn produced a marked positive reaction, but the ingestion of corn caused no untoward symptoms. Milk gave neither a cutaneous nor a clinical reaction. Ingestion of all the other constituents failed to produce any reaction.

SUMMARY

An unusual case of angioneurotic edema due to sensitivity to chicle is reported. The past history of nausea, dryness and vomiting when chewing gum, the present history of edema of the larynx together with other manifestations of an allergic response, the strongly positive cutaneous reaction to chicle extract, with mild constitutional symptoms, the positive reaction to the passive transfer test, and the elimination of the other constituents of chewing gum, allow for little doubt that chicle was the offender.

Only 2 other cases of sensitivity to chicle have previously been reported in the literature and in neither one was there laryngeal edema.

78 Irving Place

4 Kleinman, A. I. Allergy to Chicle. Preliminary Report, J. A. M. A. 104:455 (Feb. 9) 1935.

Case Reports

RECENT EXPERIENCES WITH OPERATION ON THE FACIAL NERVE

ROBERT C MARTIN, M D, SAN FRANCISCO

In 1929 a facial nerve which had been severed during a mastoidectomy was repaired by end to end anastomosis, with a good result. This procedure was reported in 1931.¹ In January 1940, the patient had good tone in the facial muscles and emotional control had improved so that the facial movements were only slightly weakened on the affected side. The frontalis muscle, however, was still inactive.

Since this first operation, 15 more patients with facial paralysis have been operated on, with 1 failure. From the cases of these 15 patients, 4 cases are chosen for presentation here as illustrative of various points.

REPORT OF CASES

The first case is of particular interest because two grafts, laid side by side, were used.

CASE 1—R W, a boy 18 months old, had had two simple mastoidectomies. During the performance of the second, on July 10, 1939, the nerve was injured, and the child awakened with a typical complete paralysis of the left facial nerve.

On Aug 3, 1939, the mastoid cavity, which still discharged, was reopened and entirely cleaned out, particularly the periantral region. The ossicles and drum were left in situ, as in a modified radical operation. The nerve was found to have been almost completely severed in its vertical portion, but a neuroma had not had time to form, indeed some fragments of the nerve were still present. It was impossible, however, to distinguish granulation tissue from nerve fibers, so the entire damaged area was excised and a graft from the sural nerve, about 15 cm long, was inserted and sutured. As an afterthought, and because the first graft seemed smaller than the trunk of the nerve, a second segment was carefully laid in, parallel to and touching the sutured graft.

The patient was dismissed from the hospital on August 23, with the left eye wide open and the left angle of the mouth drooping badly. By September 9 the corner of the mouth twitched and he pursed his lips with but slight deformity on the affected side. By September 29 the tone had so far returned to the lower branch that all drooling had ceased. On October 7 the left eye was noted to wink synchronously with the right, and by November 16 facial symmetry was restored when the face was in repose, though deformity was evident when the child cried.

From the Department of Surgery, Division of Otorhinolaryngology, University of California Medical School and the Children's Hospital.

Read at the meeting of the Western Section of the American Laryngological, Rhinological and Otological Society, Los Angeles, Jan 26, 1940.

1 Martin, R C. Intratemporal Suture of the Facial Nerve, Arch Otolaryng 13 259 (Feb) 1931.

This patient showed the most rapid return of tone and motion of all the patients in the series. After completion of treatment in this case, my attention was drawn to Bunnell's work, in which he advocated the use of cable grafts. On the basis of experiments done on cats he showed that a thick single graft undergoes necrosis, and he therefore advocated the use of cable grafts. Case 1 indicates that there is more tissue left in multiple small grafts than in one large one. The patient's age is another factor which might explain the extreme rapidity of return in this case. He was the youngest patient in the series, and, as is generally recognized, repair in youth is much more rapid than it is later.

In case 2 end to end approximation and suture were obtained, only the second case in which this was accomplished.

CASE 2—N R, a girl 6 years of age, received a deep laceration posterior to the right ear, just below the mastoid process, together with injury to the nerve, as the result of an automobile accident on Feb 22, 1938.

At operation, on May 2, 1938, the facial nerve was dissected from the surrounding bone as far as the stylomastoid foramen. Just below the foramen the nerve trunk terminated in dense scar tissue at the point of laceration. The nerve was freed, but the distal end was difficult to find, and it was necessary to go forward toward the parotid gland, pick up the fibers and work backward until the gap was found. The scar tissue between the proximal and the distal segment was excised, with a sharp cataract knife. The ends of the nerve had not been damaged and were brought together without difficulty by two fine arterial silk sutures. The wound was closed superficially with sutures of silkworm gut.

On Aug 1, 1938 a return of tone, with lessened sagging on the right side, was noted. The child was not seen again until April 1939, when she could close the eye and move the right side of the face well except the frontalis muscle. In October 1939 this muscle was found to be reacting slightly.

It is of interest to note that this is the only case in the series in which the frontalis muscle has resumed its function. This may be accounted for by the end to end anastomosis and the early operation.

The third case is of interest because of the bizarre manner in which the injury occurred and the fact that it probably obliterated the jugular vein near the bulb.

CASE 3—G B, a man 60 years of age, was injured on May 28, 1938, with a 22 caliber bullet fired at the base of the skull. The bullet skidded around the occipital bone and buried itself just in front of the mastoid process. The patient presented himself in July 1938 with complete paralysis of the right facial nerve. The scar of entry of the bullet was visible, and the bullet showed plainly on the roentgenogram.

Operation was performed on July 13, 1938. When the mastoid process was exposed, the bone under the periosteum looked dark and the cells were seen to be filled with old blood and pigment. The cells were removed, and the tip of the mastoid process was found to have been fractured by the bullet. The facial nerve was exposed along the facial canal. From the stylomastoid foramen to near

2 Bunnell, S, and Boyes, J H. Nerve Grafts, *Am J Surg* 44:64 (April) 1939.

the horizontal canal the nerve was dark. Several fragments of lead were removed from the nerve at a point just below the emergence of the chorda tympani. About 2 cm. of fibrous nerve tissue was removed, part of this being the low vertical portion of the nerve and part of it the portion lying in the soft tissue in the forward course of the nerve toward the parotid gland. Except for discoloration, the nerve appeared to be normal below and above the segment removed. The bullet was found medial and slightly anterior to the foramen, being in or near the jugular bulb. It was worked loose and removed, but the expected gush of blood did not follow, although the bullet must have penetrated the region of the bulb. A suitable segment from the right saphenous nerve was removed and sutured into position with fine arterial silk. The wound was closed with catgut sutures and the skin with clips.

Three weeks after operation the patient returned to his home in Oregon and was not seen until May 12, 1939. At that time he was able to close the right eye and to move the right corner of the mouth. The muscle tone was good. In a letter dated December 5, 1939 this patient wrote, "My eye and ears have both been improved considerably since spring. My face to all appearances is normal. There is still a stiffness of the muscle of my face."

I was unable to obtain satisfactory photographs for demonstration, as the patient did not remain in San Francisco long enough in May and the snapshots he sent were useless for reproduction.

In case 4 repair was accomplished on the eighth day after injury.

CASE 4—W. J., a boy 2 years of age, was injured during a simple mastoidectomy on March 5, 1937.

Repair was done on March 13. The wound was revised at this operation, and all drainage promptly ceased. It was found that the nerve had been injured in its vertical portion just below the horizontal canal. It was therefore necessary to free the nerve in its canal below the horizontal portion, the drum and ossicles being gently moved forward while this was accomplished. About 1 cm. of nerve was resected, and a graft from the sural nerve was inserted and sutured with arterial silk.

On April 21 the muscle tone had improved. By June 2 the boy could close the right eye, and by July 28 the face was perfectly symmetric in repose and there was a mere suggestion of return of function in the frontalis muscle, so slight as to be barely perceptible.

Apparently no more necrosis occurred in this graft than might be expected in an uninfected wound.

COMMENT

It has been my contention previously that operation should be delayed until the field is entirely healed and free from infection. I am still inclined to this opinion, although in 2 of the 4 cases presented (cases 1 and 4) the operation was performed while discharge was still present in the middle ear. In neither case was more difficulty encountered than in the presence of a clean field. In both the results were good.

In all cases in which operation is performed on the facial nerve the postoperative procedure is to mop out any serum which may appear on the external surface of the anicle. This is done gently, and the canal is never entered. Protective dressings are not used over the graft or suture line, nor is the wound or the graft inspected after operation. Strong chemicals, of course, should not be used. I have had no experience in laying the grafts in position, but have always sutured them as accurately as possible. This, perhaps, accounts for the fact that I do not feel it necessary to have protective covering over the graft and the adjacent nerve.

The question arises as to what loss of hearing may be expected, since some disturbance of the drum and ossicles is inevitable. In all those patients for whom it was necessary to dissect some of the horizontal portion of the nerve there has been a slight loss as measured by the audiogram, but it has not been so marked as was anticipated. In this connection, too, an interesting fact was noted during the convalescence of the patient with the gunshot wound (case 3). He complained that his hearing seemed dull but that loud noises bothered him, a finding indicative of injury to the stapedial nerve. The complaint lasted about two months and then disappeared. The same thing occurred in a patient on whom I operated early this month. Regeneration of the stapedial nerve is the only explanation which occurs to me. This seems to confirm experimental work on the function of the stapedius muscle.

All of our cases demonstrate that the return of function after the repair of a damaged facial nerve is not perfect, because associated movements occur and because in almost all instances the frontalis muscle fails to act. Recently Fowler³ summed up the knowledge of abnormal movements following injury to the facial nerve. He noted that in all cases of severe injury to the facial nerve, associated movements of various parts of the face occur after recovery. He also mentioned the ticlike movements which occur in patients with healed facial palsy of traumatic origin if they blink their eyes frequently or have mobile faces. He said further that these phenomena are caused by splitting of axons in the neuroma so that one axon enervates several parts of the face. There may be some question as to whether this explanation is correct, but it is the most plausible advanced so far. I have had only 2 patients in whom the ticlike movements were troublesome or even apparent. Both of these were children, 1 of whom had an early repair (eight days after injury) and the other a late one. In the first mentioned the severed ends of the nerve were placed in apposition. The tic was severe for two years, but when this child was seen on Jan 5, 1940 it had completely disappeared. The operation was performed early in 1936. The patient with the late repair (one year after injury) had a decompression of the nerve. Troublesome tics of the muscles about the mouth and cheek occurred. After two and one-half years they are diminishing in frequency and intensity. These 2 cases suggest that the tics may all disappear in time.

3 Fowler, E. P. Abnormal Movements Following Injury to the Facial Nerve, *J. A. M. A.* **113** 1003 (Sept 9) 1939.

SUMMARY AND CONCLUSION

1 Despite the fact that return of function is not perfect, as described in the case reports, the improvement in the appearance of the patient, particularly when the face is in repose, is so marked that the operation is worth while

2 In intelligent patients who are old enough to cooperate, I have been able by means of long practice to restore partial emotional control of acts such as smiling

3 The only return of function of the frontalis muscle occurred in a patient who had an end to end suture of the nerve without an intervening graft

4 It is probable that the facial tics which may follow trauma to the facial nerve will disappear after a few years

Dr Howard A Brown, of the Department of Surgery, assisted in the handling of a number of these patients

ANGIOENDOTHELIOMA OF THE NASOPHARYNX

W D FARMER, M D, DURHAM, N C

An angioendothelioma is an angiomatous tumor composed of blood vessels in early stages of formation and possessing low grade malignancy¹ Golgi is credited as being the first to use the term endothelioma, in 1869 and Maurer² in 1879 described 2 cases of slowly growing malignant tumors composed of ingrowth from endothelial lining of blood vessels, which he called angiosarcoma Franke³ a year later described a tumor of tissue and blood spaces lined with endothelial cells, which he preferred to call endothelioma rather than sarcoma Boist⁴ stated that angioendothelioma is clinically rather benign, although it does cause local destruction of tissue and recurs when removed According to Geschickter and Keasbey,⁵ when active proliferation occurs in capillary angiomata in which masses of endothelial cells are seen about the vascular channels, a subvariety of these tumors, angioblastic hemangioma, is created They are sometimes called hemangioendothelioma and are difficult at times to distinguish microscopically from sarcoma

Angiomatous tumors are frequently found, but only a small percentage of these can be classified as angioendotheliomas In an analysis of 200 cases of neoplasms of the blood-lymph-vascular system Pulford⁶ found only 9 cases, or 4.5 per cent Angioendothelioma of the nasopharynx is rather unusual Salinger and Pearlman,⁷ in a study of 24 cases of tumor of the epipharynx, reported 1 case of endothelioma, in which the cells were arranged in clusters and channels surrounding small blood spaces, in some areas they proliferated, obliterating the lumen Crowe and Baylor⁸ reported cases of angiosarcoma of the

From the Department of Otolaryngology, Duke University Hospital and Medical School

1 Bell, E T Textbook of Pathology, ed 3, Philadelphia, Lea & Febiger, 1938, p 283

2 Maurer, F Ein Beitrag zur Kenntnis der Angiosarcome, Virchows Arch f path Anat **77** 346, 1879

3 Franke, F Endothelioma intravasculare hyalogenes der Submaxillargegend Virchows Arch f path Anat **121** 465, 1890

4 Borst, M, in Aschoff, L Pathologische Anatomie, ed 7, Jena, Gustav Fischer, 1928, vol 1, p 753

5 Geschickter, C F, and Keasbey, L E Tumor of Blood Vessels, Am J Cancer **23** 568 (Feb) 1935

6 Pulford, D S Neoplasms of the Blood-Lymph-Vascular System, with Special Reference to Endotheliomas, Ann Surg **82** 710 (Nov) 1925

7 Salinger, S, and Pearlman, S T Malignant Tumors of the Epipharynx, Arch Otolaryng **23** 149 (Feb) 1936

8 Crowe, S J, and Baylor, J W Benign and Malignant Nasal Growths, Arch Surg **6** 429 (March) 1923

nasopharynx but none of angioendothelioma. Other forms of angiomatous tumors, such as cavernous angiomas and angiofibromas are more commonly found in this area.

Pulford⁶ expressed the opinion that angioendothelioma represents the intermediate stage between the strictly benign angioma and the malignant endothelioma. The characteristic pathologic picture of angio-

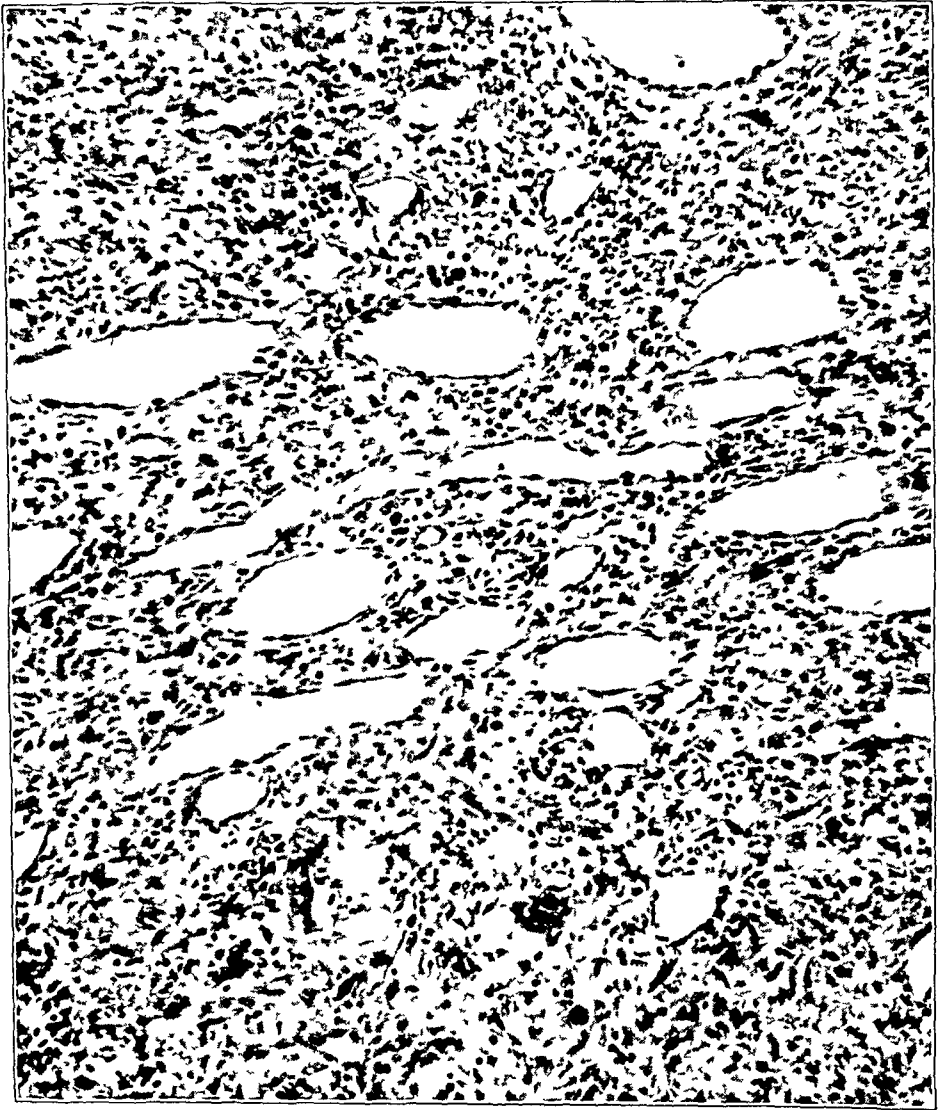


Fig 1—Low power photomicrograph showing the general structure of the tumor, with a large number of blood sinuses.

endothelioma is recognized as essentially that of blood spaces and vessels in which endothelial cells tend to grow into the sinuses as small buds. The tumor, although relatively benign, tends to recur when removed, is mildly invasive and shows occasional mitotic figures. There are rarely any distant metastases. Excellent response of angioendo-

thelioma to roentgen and to radium irradiation is recorded. When possible, local excision should be carried out and followed by irradiation.⁹

The growth in the case reported here presented the characteristics of angioendothelioma in that it recurred after removal, was locally invasive and destructive of soft and bony tissue and showed the typical histologic picture. The case is unusual owing to the location of the lesion.



Fig 2—High power photomicrograph of a portion of the section shown in figure 1, showing endothelial lining of the blood sinuses

9 (a) Sweeter, S. E., and Winer, L. H. Hemangio-Endothelioma, *Arch Dermat & Syph* **34** 997 (Dec.) 1936. (b) Rice, C. O. Hemangio-Endothelioma of the Thyroid Gland, *Am J Cancer (supp)* **15** 2301 (July) 1931. (c) Dewitt, C. H. Hemangio-Endothelioma. A Case, *Radiology* **23** 335 (Sept.) 1934.

REPORT OF A CASE

E M, a 27 year old white housewife, entered the hospital on Jan 2, 1933, complaining of a growth in the throat. About a year before, she had noticed that there was difficulty in breathing through the nose and that her speech was affected. The symptoms grew worse until she was barely able to breathe through the mouth, on account of the size of the growth in the nasopharynx, which pushed the soft

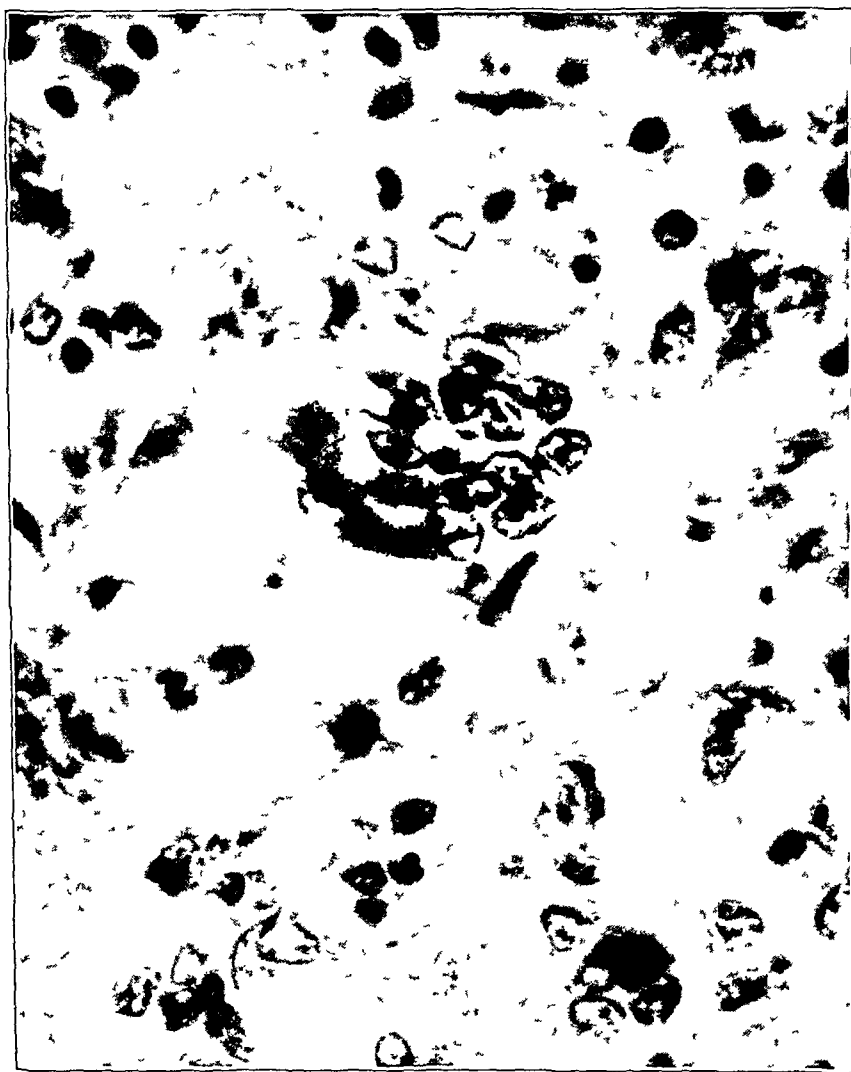


Fig 3—High power photomicrograph showing giant cells of the tumor

palate forward. She consulted a physician, who removed the growth, and for a few months she was able to breathe well again. Because of recurrence of the growth, she was referred to Duke University hospital for treatment. The growth produced the same symptoms as before. In addition, there had been symptoms of fulness in the ears for the past year.

The past history showed that four years previously there had been an attack of pain and stiffness in the neck, which soon involved the other joints of the body. Subsequently a mass the size of an egg appeared in the back of the neck, which suppurated and was surgically drained. Two years previously tonsillectomy

had been performed, with local anesthesia. Lymph nodes of the neck became enlarged and tender after the operation, but the swelling soon subsided.

The marital and the family history were entirely irrelevant.

Examination—Physical examination revealed a thin, poorly nourished and underdeveloped woman, who breathed entirely through the mouth. There was a "nasal" quality to the voice. The cervical lymph nodes were greatly enlarged but not especially tender. There was considerable stiffness and discomfort on passive motion of the cervical portion of the spine. The nose was filled with mucopurulent discharge, and after this was removed by suction a tumor mass was seen projecting into both nares posteriorly. The nasopharynx also was completely filled with the mass. Examination of the pharynx showed the soft palate bulging forward, because



Fig. 4—Lateral roentgenogram showing partial destruction of the body of the second cervical vertebra, as well as anterior collapse and kyphosis.

of a chocolate-colored mass, firm and rubbery, which projected about 1 inch (2.5 cm) below the soft palate. The mass was slightly movable but no pedicle could be demonstrated. The tumor bled readily. There were a few patches of exudate on the surface of the mass. Results of the remainder of the general physical examination were essentially normal.

The Wassermann reaction of the blood was normal. The leukocytes numbered 13,000, with a normal differential count. The hemoglobin value was 90 per cent. Roentgen studies of the sinuses and chest were normal. Unfortunately, lateral roentgenograms of the neck were not made at this time.

Operation—With the patient under light ether anesthesia, the tumor, which measured approximately 3 by 4.5 by 6 cm, was removed by blunt dissection, mainly with the finger. Venous bleeding was free but readily controlled during the operation. The tumor was the shape of a dumbbell, about half of the mass being beneath

the mucosa. The removal of the tumor left a crater-like defect, in the floor of which the anterior cervical vertebrae were palpated and found to be roughened and eroded. The pathologic studies of the tumor are reported a little later in this paper.

Course—The postoperative course was complicated by a rather severe fusospirochetal infection of the wound, which cleared up under arsenical therapy and local treatment.

After the patient's recovery from the operation, roentgen and radium therapy were applied to the nasopharynx. Postoperatively she had considerable earache, which was entirely referred. However, a bilateral mastoid operation was done the day following discharge from our hospital.

Since operation the patient has been followed at intervals, and there has been no evidence of recurrence of the tumor. There is considerable scarring of the pharynx and nasopharynx. A roentgenogram of the cervical part of the spine taken five months after operation showed some destruction of the body of the second cervical vertebra, together with collapse and impingement of the spinous process on that of the third (fig 4). The latest roentgenogram, however, showed some regeneration of the bone in the region of the first and second cervical vertebra. At present the patient is enjoying good health, her only complaints being stiffness of the neck and occasional pain on turning her head. At no time has she shown evidence of pulmonary tuberculosis.

Pathologic Studies—Gross. The specimen consisted of several parts, the largest of which measured 4 by 2.5 cm. There were several smaller fragments. The characteristic type of tissue making up this tumor was dark reddish, somewhat soft, rubbery and gelatin-like. The tissue was friable and did not appear vascular. Little or no blood could be expressed from the tumor on pressure. The largest piece of tumor was covered on the outside by a rough white capsule of fairly tough, dense fibrous tissue.

Microscopic. Numerous blocks made from this tumor all presented the same characteristic picture. The capsule that was apparently covering the entire tumor was composed of a thick, rather vascular connective tissue. The tumor proper was made up of a hyaline vascular structure of large blood sinuses lined with a single layer of endothelial cells supported by scanty stroma (fig 2). The sinuses in the section were filled with blood (fig 1). There was a marked tendency for the cells to grow into the sinus as small buds, forming multinucleated giant cells still attached to the wall (fig 3). The nuclei making up these giant cells were distinctly endothelial in origin. The cells were uniform, having reticulated nuclei and a pinkish granular cytoplasm. The most striking feature in the sections was the large number of giant cells. There were few, if any, mitotic figures.

COMMENT

The lesion in the case reported appears to fit into the class of angioendothelioma. The microscopic sections showed the characteristic pathologic picture of proliferation of endothelial cells of the blood spaces as buds and giant cells. The recurrence of the tumor, together with its tendency to invade and destroy tissue and bone, was characteristic of this type of growth. It apparently was of low grade malignancy, and there were no metastases. After surgical removal there was excellent response to irradiation therapy.

SUMMARY

A case of angioendothelioma of the nasopharynx is reported. Photomicrographs of the tumor and a lateral roentgenogram of the cervical vertebrae accompany the report.

BLASTOMYCOSIS OF THE ESOPHAGUS

GERHARD D. STRAUS, M.D., MILWAUKEE

Resident Physician in Otolaryngology, Milwaukee County Hospital

Since blastomycosis was first described by Gilchrist in 1894, several hundred cases have been reported in the literature. In only 3 of these has there been involvement of the esophagus. Shepherd and Rhea¹ and Martin and Smith² have reported 2 cases, respectively, in which esophageal lesions were demonstrated at postmortem examination of patients with systemic blastomycosis. Vinson, Broders and Montgomery³ reported a case of esophageal involvement which was noted clinically and proved by the use of the esophagoscope together with biopsy, unfortunately, however, the patient died one year later and autopsy was not obtained.

Much confusion has existed as to the classification of the causative organism. Most observers have limited the term blastomycosis to the lesions caused by a circular, double contoured, yeastlike organism 10 to 18 microns in diameter with a granular cytoplasm and characterized by the ability to produce buds in tissue and mycelium when cultured on Sabouraud's medium.

The lesions themselves resemble those of tuberculosis grossly and histologically. When they occur in the skin, they are of a raised granular appearance with ulceration and small abscess formation. Histologically, the organisms may be identified in an environment of chronic inflammatory tissue which differs from areas of tuberculosis in that there is no caseation necrosis. Giant cells are always present and frequently contain the offending organism. Lymphocytes, epithelioid cells and fibroblasts dominate the picture, and occasional areas of polymorphonuclear infiltration with milium abscess formation may be found.

Clinically, two types of the disease have been recognized: a cutaneous and a systemic type. In the cutaneous type, the lesions are few and on the exposed portions of the body.

In the systemic type, severe multiple dermal lesions are usually present, as well as frequent involvement of the lungs. Lesions of the bone, kidney, spleen, genitals and larynx are not uncommon. Lesions of the gastrointestinal tract are rare.

From the Department of Otolaryngology, Marquette University School of Medicine and Milwaukee County Hospital.

1 Shepherd, F. J., and Rhea, L. I. A Fatal Case of Blastomycosis, *J. Cutan. Dis.* **29** 589, 1911.

2 Martin, S., and Smith, D. T. (a) Blastomycosis. A Review of the Literature, *Am. Rev. Tuberc.* **39** 275 (March) 1939, (b) Blastomycosis. A Report of Thirteen New Cases, *ibid.* **39** 488 (April) 1939.

3 Vinson, P. P., Broders, A. C., and Montgomery, H. Blastomycosis of the Esophagus, *Surg., Gynec. & Obst.* **46** 255 (Feb.) 1928.

The portal of entry of the organism is not definitely known, though it is felt that the fungi frequently gain entrance through a superficial abrasion of the skin. Cases of primary lesions occurring in such abrasions have been reported by Toepel,⁴ McKenty and Morgan⁵ and Robinson⁶

Evans⁷ reported a case of a primary lesion developing in a puncture wound sustained by a physician performing an autopsy on a person with systemic blastomycosis



Fig 1—Barium sulfate esophagogram, showing the constriction in the upper third of the esophagus and dilatation above

The diagnosis can best be made by a biopsy of the lesion or by smear and culture of the organism. Martin and Smith^{2a} suggested complement fixation and intradermal tests, these tests, however are not diagnostic

4 Toepel, T. Systemic Blastomycosis, *J A M A* **93** 32 (July 6) 1929

5 McKenty, F. E., and Morgan, D. Blastomycosis, *Ann Surg* **61** 513 (May) 1915

6 Robinson, H. M. Blastomycotic Dermatitis by Lymphatic Extension, *Arch Dermat & Syph* **28** 219 (Aug) 1933

7 Evans, N. A Clinical Report of a Case of Blastomycosis of the Skin from Accidental Inoculation, *J A M A* **40** 1772 (June 27) 1903

The disease must be differentiated from other mycotic infections, tuberculosis, syphilis and malignant growths. In the esophagus it most closely resembles carcinoma, both clinically and roentgenographically.

The treatment of the cutaneous type with potassium iodide or irradiation is usually successful, but there is no effective treatment for the systemic type.

REPORT OF A CASE

A 61 year old Negro, a laborer, entered the Milwaukee County Hospital on Oct 18, 1939, complaining of progressive dysphagia of two years' duration. He formerly had been observed at the outpatient department of that hospital for granulomatous cutaneous lesions on the nose and lower lip, which began four months previously as a small papule in the corner of the mouth. Though advised to return for biopsy and further study, he failed to submit to these procedures until the time of his admission to the hospital three months later.

Four years before, a positive Wassermann reaction of the blood and spinal fluid had been found, and intermittent antisyphilitic treatment was given for five months, reversal of the Wassermann reaction being achieved.

Examination—Results of physical examination were irrelevant except for emaciation and dirty white, elevated lesions of a granular appearance about 2 by 3 cm and 1.5 by 2 cm, which were noted on the skin of the nose and lower lip respectively. The report made by Dr John Grill on the biopsy of the lesion on the lower lip was of blastomycosis. A roentgenogram of the chest was normal. An esophagogram made with the aid of barium sulfate revealed an almost complete constriction in the upper third of the esophagus, allowing the passage of only a thin barium mixture (fig 1).

Results of the blood count were as follows: hemoglobin 71 per cent, red blood cells 4,450,000 and leukocytes 5,600, with segmented forms 70 per cent, stab forms 5 per cent, lymphocytes 22 per cent, monocytes 2 per cent and eosinophils 1 per cent. The sedimentation rate was 81 mm in one hour.

Esophagoscopy at this time revealed a soft, granular, constricting lesion which was annular and located 6 cm below the cricopharyngeus muscle. Slight trauma produced bleeding. Biopsy showed chronic inflammatory tissue.

Course—Three days later complete obstruction occurred and gastrostomy was performed.

Biopsy of material taken during a second esophagoscopy procedure demonstrated chronic inflammatory tissue in which were found typical blastomycotic organisms (fig 2). Smears and cultures of tissue taken directly from the lesion revealed no organisms.

Despite the normal roentgenographic appearance of the chest and normal results of examinations of sputum, direct laryngoscopic and bronchoscopic procedures were deemed advisable. No gross pathologic condition was demonstrated, and smears and cultures of material taken directly from the larynx and bronchi yielded no growths.

After treatment with large doses of potassium iodide, the cutaneous lesions healed and the dysphagia seemed for a time to lessen. Two weeks before the patient's death, however, the obstruction increased and feedings were resumed through the gastrostomy tube. Esophagoscopy was performed, and a No. 16 French esophageal bougie was passed through the obstruction. The clinical course, however, was progressively downhill, and the patient died on Feb 7, 1940.

Autopsy—Postmortem examination performed by Dr John Grill revealed the following findings. The body was emaciated. Over the left ala nasi was a retracted gray scar 3 cm in diameter. A scar of similar type was on the lower lip near the left angle of the mouth. The eyes were normal. A gastrostomy opening was present. The genitals were without external change.

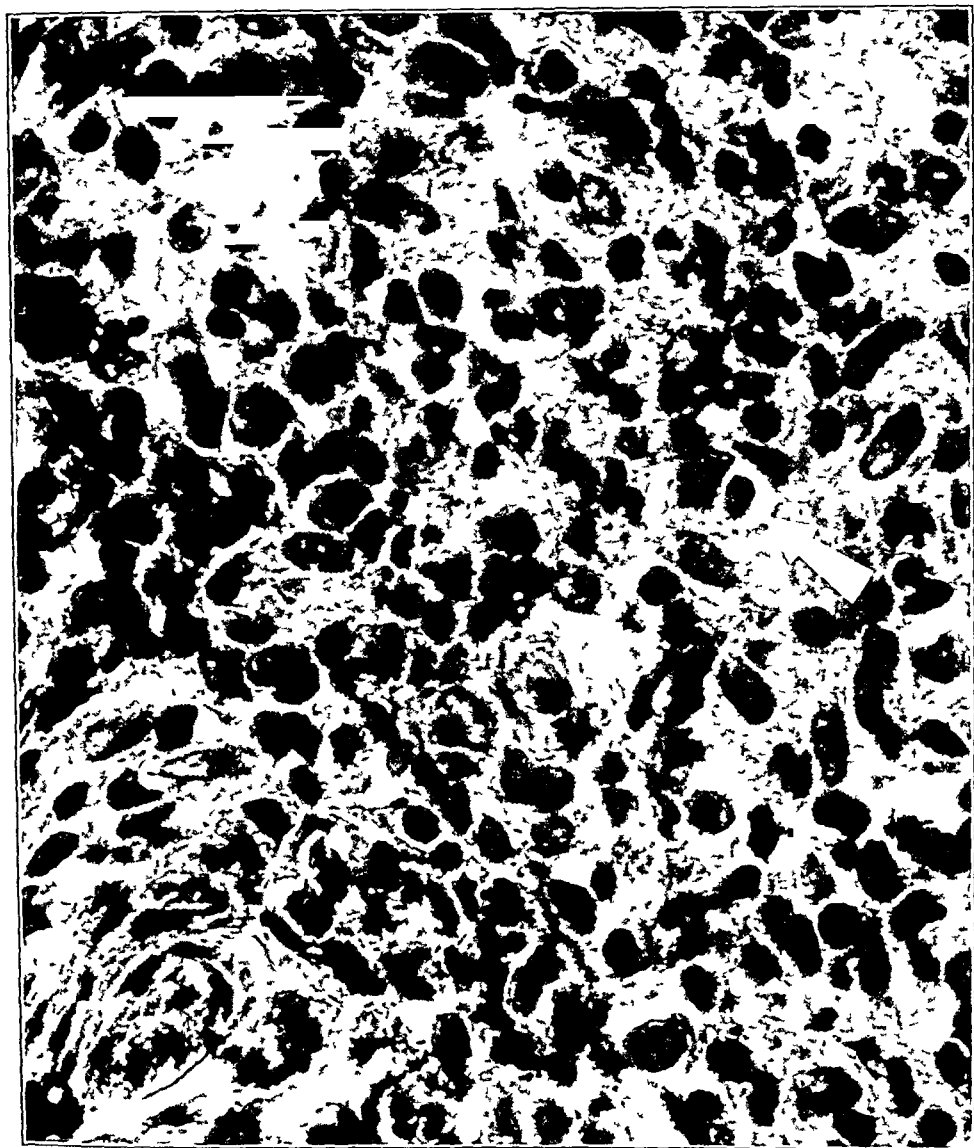


Fig 2—Photomicrograph of a biopsy specimen removed from the esophagus, showing chronic inflammatory changes. A giant cell may be seen. A typical double-contoured blastomycetic organism is indicated by the arrow.

The pharyngeal portion of the esophagus was dilated. When it was attempted to pass one blade of the scissors through the lumen of the esophagus, an obstruction was encountered about 5 cm distal to the cricoid cartilage caused by a large annular mass 9 cm long. The border was fairly well defined and blended with the normal esophageal wall. The more proximal portion of the lesion was

formed by a crater 3 cm in diameter. Its edges were slightly elevated and indurated. Its base was smooth and glistening white. Distally from this area were several small, raised, tubercle-like structures, grayish white and 2 to 3 mm each. The lower portion of the lesion showed complete erosion of the mucous membrane and a smooth surface. Section showed the wall to be considerably thickened, the inner aspect being fibrous and measuring 3 mm. The outer portion was more congested and also measured 3 mm (fig 3).

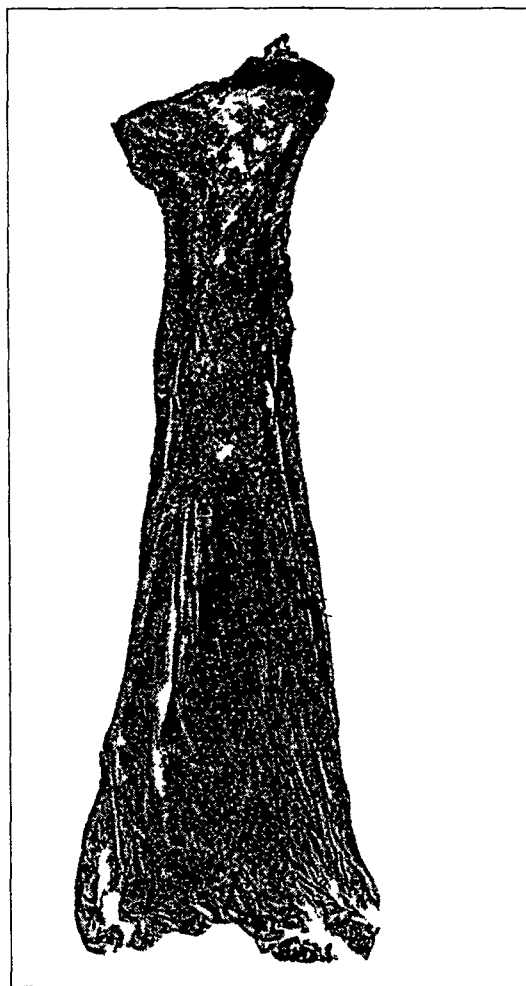


Fig 3—Gross specimen of the esophagus removed at autopsy, showing the ulceration and tubercle-like elevations. The marked thickening of the wall is to be noted.

The bronchi showed atrophic changes. The lungs were edematous and emphysematous and showed no evidence of blastomycosis. The tracheobronchial lymph nodes were also free of blastomycotic change.

The musculature of the heart showed evidence of brown atrophy. In the ascending portion of the aorta, above the leaflets, were sunken porcelain-like areas. Above these areas were hyalinized plaques. These changes were interpreted as beginning syphilitic aortitis.

The liver, gallbladder, spleen, kidneys, urinary bladder, adrenal glands, prostate gland, testes and epididymis were essentially without pathologic change

The stomach showed the gastrostomy opening. The rest of the gastrointestinal tract was normal.

Histologic examination of these organs showed no blastomycosis, the esophagus being the only site of the disease.

COMMENT

Esophageal obstruction due to local blastomycosis is a rare condition. However, since it can occur it must be considered in the differential diagnosis of obstructive lesions, especially since in the barium esophagogram it may so closely simulate carcinoma.

It is a matter of speculation as to whether the lesion in the reported case spread from the esophagus to the skin or vice versa. However, since dysphagia was the first symptom, preceding the cutaneous lesions by about one and one-half years, and since autopsy revealed no involvement of contiguous cervical and mediastinal structures which might suggest an infiltrating invasion, one may be justified in assuming that the primary inoculation occurred in an esophageal abrasion and produced a local lesion which may be likened to a typical cutaneous lesion. The lesions of the face were probably caused by an inoculation of sputum containing the organisms into an abrasion in the skin.

In the 2 cases reported by Shepherd and Rhea¹ and Martin and Smith,^{2b} autopsy revealed widespread metastases with marked involvement of the mediastinal lymph nodes, so that while in their reports no reference is made as to the mode of invasion, it is likely that the esophageal lesions developed by an invasion of the disease from the involved mediastinal structures.

The lesion reported by Vinson, Biodeis and Montgomery³ showed a roentgenographic and esophagosopic picture similar to that in the case reported here. Their patient, however, had advanced bilateral pulmonary tuberculosis, and since autopsy was not performed one cannot be sure that the esophageal lesion was purely local.

SUMMARY

A case of local blastomycosis of the esophagus is presented, together with a brief review of the literature and a summary of the present concept of the disease.

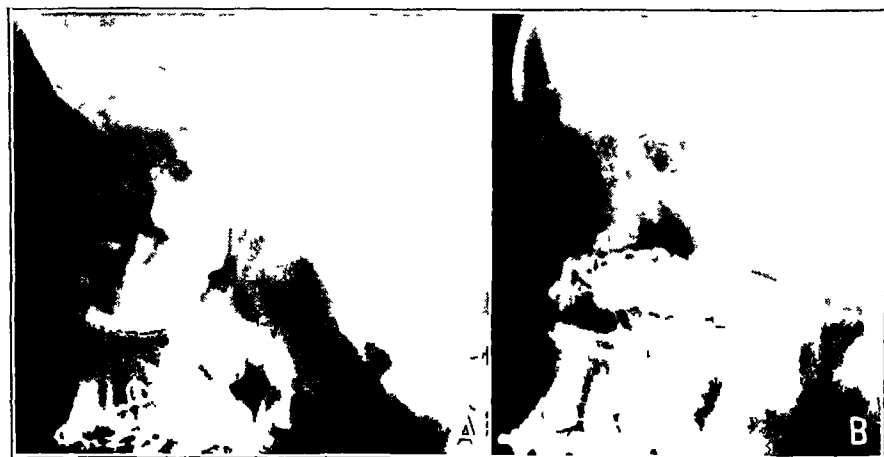
CONGENITAL ATRESIA OF POSTERIOR NARES

A MANGIARACINA, M D, BROOKLYN

I should like to report a case of congenital atresia of the posterior nares, in which operation was performed and patency achieved

On May 7, 1938, M C, aged 11 years, presented herself with a history of nasal obstruction and nasal discharge since birth Examination revealed a septal deviation almost completely occluding the left nasal chamber The right nasal chamber was roomy The nose was full of mucoid secretion An applicator placed in each side of the nose failed to enter the nasopharynx A colored solution instilled into each nostril also failed to come through

Posterior rhinoscopic examination with a Beck nasopharyngoscope introduced through the mouth showed a normal outline of the posterior nares and of the posterior extremity of the septum, but a few millimeters anteriorly a septum



A, roentgenogram made on May 14, 1938, showing complete atresia of the posterior end of the nasal cavity, *B* roentgenogram made on Jan 5, 1940, about eighteen months after operation, showing the patency of the posterior nares

occluded both openings completely The palatal arch was high There were corrective appliances on the teeth The tonsils were enlarged A roentgenogram taken May 14, 1938, after the insertion of iodized oil, demonstrated complete atresia at the posterior end of the nasal cavity

Operation—Under general anesthesia the patient was operated on at the Brooklyn Eye and Ear Hospital on June 17, 1938 A semilunar incision was placed on the left side of the septum at the mucocutaneous junction, and the mucoperichondrium and periosteum were elevated from the left side The cartilage was next incised, and the perichondrium and periosteum were elevated on the right side of the septum The deviation of the septum was partially corrected, and the separation of the mucoperiosteum was continued posteriorly and laterally on each side of the septum until the nasal surface of the choanal obstruction was visible The bony outline of the posterior nares was normal, but the openings were closed

by a thick fibrous membrane. The removal of the vomer was continued through the posterior edge, the bony septum between the choanal openings thus being destroyed. The fibrous wall was removed from its attachment. An incision was then made through the elevated mucoperiosteum on each side of the septum near the posterior extremity, a large opening resulting. A tampon was placed in the postnasal space. The new opening was packed with petrolatum gauze. Both sides of the septum were packed with strips of petrolatum gauze.

On June 18 the nasal strips and postnasal tampon were removed. The packing in the new opening was left in two days longer and then removed. Bleeding was negligible at all times.

The patient was discharged from the hospital on June 21.

On July 1 a large opening was visible posteriorly.

On July 15 the patient was discharged as cured but was told to report from time to time.

On Dec 26, 1939 posterior rhinoscopic examination with a nasopharyngoscope introduced through the nose showed a large opening into the nasopharynx. The posterior edge of the septum was crescentic.

On Jan 5, 1940 a finger cot containing a strip of plain packing impregnated with iodized oil was placed into the nose and made to project into the nasopharynx, and a roentgenogram was taken to show the patency of the posterior nares.

MUCOCELE OF THE FRONTAL SINUS

J A WEISS, M D, CHICAGO

Mucocele of the nasal accessory sinuses, though not rare, is relatively uncommon and of clinical interest because of its varied features. In this report 2 cases will be described, 1 of which presents some noteworthy findings. Also, the more recent concept of the formation of a mucocele will be emphasized.

St Clair Thomson and V E Negus defined a mucocele as "an accumulation of a mucous secretion within an accessory sinus with distention of one or more of its walls. This secretion may be loculated in one part of the sinus and may become purulent, when it is called a pyocele. It is generally associated with more or less obstruction in the outlet of the cavity, and it may be caused by blockage and cystic dilatation of a gland"¹. The lesion occurs most often in the frontal and ethmoid sinuses, less frequently in the antrum and rarely in the sphenoid sinus.

In a consideration of the mechanism of formation of a mucocele two factors must be thought of: (1) closure or narrowing of a sinus ostium—usually the nasofrontal duct—due to osteoma or some other benign neoplasm, trauma, congenital abnormality or inflammation, and (2) cystic dilatation of a gland or cystic degeneration of a polyp. That initial closure of the ostium is not essential is indicated by many cases in which it does not occur. The older view of accumulation and retention of mucoid secretion following blockage of a sinus outlet does not explain the occurrence in all cases. Even in the absence of an obstruction to the ostium a glandular retention cyst may fill the entire cavity of a sinus. This type of degenerative process on a chronic inflammatory basis is very likely the major factor in the development of a mucocele.²

After eliminating dental cysts from his discussion, Hardy stated that there is no essential difference between a retention cyst of the antrum and a mucocele, as both are lined by columnar or cuboidal epithelium. A cyst, however, usually contains a thin fluid, in contrast to the thick contents of a mucocele. Hardy maintained that mucocele is a clinical term rather than a designation of a pathologic entity.³ Carrying this thought further, one may find it convenient to apply the term retention cyst to a circumscribed saccular swelling and to limit the designation

From the Illinois Eye and Ear Infirmary

Read before the Chicago Laryngological and Otological Society, Dec 4, 1939

1 Thomson, St C, and Negus, V E. *Diseases of the Nose and Throat*, ed 4, New York, D Appleton-Century Company, Inc, 1937, p 286

2 Lobell, A. Relationship Between Mucocèles and Cysts. Report of Cyst of Maxillary Sinus, *Arch Otolaryng* 6:546 (Dec) 1927

3 Hardy, G. Benign Cysts of the Antrum, *Ann Otol, Rhin & Laryng* 48:649 (Sept) 1939

of mucocele to those cysts which have a viscid secretion and have expanded to occupy the entire sinus cavity, with or without distention of the bony walls

SYMPTOMS

The signs and symptoms of a mucocele depend on the size of the swelling and on the pressure effects on adjacent structures. In the earliest stage the sinus wall may be intact, later it is distended and softened, giving a "parchment-like" crackling on palpation. Erosion through the floor of the frontal sinus permits presentation of a globular elastic swelling at the inner orbital angle. Growth is slowly progressive and usually painless.⁴

Ocular symptoms are prominent. The eye is displaced forward, downward and laterally. Diplopia, ptosis of the lid, epiphora, limited movement of the globe and a variable degree of impaired vision may be present.

Intranasal changes are exceptional. Occasionally, infection leads to the formation of a pyocele, with signs of acute inflammation.

The roentgenographic appearance has been well described by Wachowski and Hartung, as follows:

The roentgen findings parallel the pathological picture. In early cases, there may be no characteristic findings. Most cases, however, first come under observation when the process has advanced sufficiently to present findings which are fairly distinctive. These include variations in density of a positive or negative nature in connection with the sinuses and abnormalities of contour and structure of the walls of the sinuses. The changes depend upon the size, shape and location of the mucocele and the extent to which it has produced pressure effects in the form of erosion, displacement, or reactionary changes in the surrounding structures.

When the distending fluid has begun to cause bone changes, the roentgen findings are quite characteristic. The gross outline is usually slightly larger than that of the other side, and there is decreased density over the sinus. The borders lose their septate or scalloped appearance and the marginal densities become rarefied, smooth and regular, which is perhaps the most characteristic finding.

The orbital roof may be flattened and a defect be seen in it. A lateral exposure may reveal considerable unsuspected encroachment upon the anterior cranial fossa. There may be areas of increased density along the margins of the sinus, which represent reactionary bone formation.

Although the fluid filled cyst is less radiolucent than the normal air filled sinus, this added density is more than offset by the secondary erosion of the walls caused by the expanding cyst. Increased densities are suggestive of the condition only when accompanied by secondary changes of surrounding structures or if localized within the sinus, as in the cases of small retention cysts.⁵

REPORT OF CASES

CASE 1—M. H., a woman aged 62 years, was seen on June 4, 1936 at the Illinois Eye and Ear Infirmary because of a large swelling of the left upper

⁴ Howarth, W. G. Mucocele and Pyocele of the Nasal Accessory Sinuses, *Lancet* 2 744 (Oct. 8) 1921.

⁵ Hartung, A. and Wachowski, T. Mucocele of the Frontal Sinus, *Am J Roentgenol* 34 30 (July) 1935.



Fig 1 (case 1) —Elastic swelling of the left lid and of the left side of the forehead, slowly progressive for six years The spheroid mass measured 10 by 8.5 by 6 cm



Fig 2 (case 1) —Anteroposterior roentgenogram, showing considerable opacity of the left frontal sinus. The gross outline is increased The upper margin shows increased density due to proliferative activity The orbital roof and the anterior sinus wall are absent The right frontal sinus is cloudy

eyelid and of the forehead. This had been slowly progressive in the past six years. There was no definite history of trauma. Dull headaches were present at intervals. There were nasal discharge and crusting.

The mass was tense, elastic and painless, and the surface was traversed by several large veins. It was roughly spheroid, extending from the upper lid over the temporal and the frontal area. The transverse diameters were 10 and 8.5 cm, and the elevation above the plane of the frontal bone was 6 cm. The lids could not be opened voluntarily, and the eye was displaced downward and laterally with considerable proptosis (fig. 1).

Examination of the left eye showed injection of the conjunctiva, a normal cornea and cloudiness of the anterior chamber preventing visualization of the fundus.

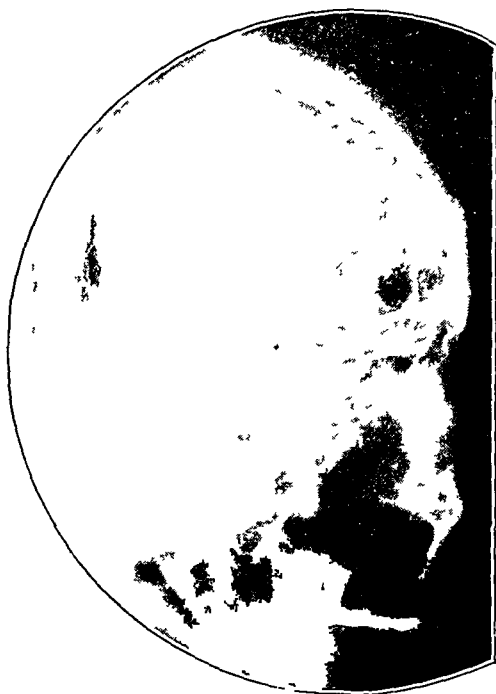


Fig. 3 (case 1)—Lateral roentgenogram showing the unusual depth of the frontal sinus, due to backward extension in the orbital plate of the frontal bone.

The ocular movements were limited, and there was no perception of light. The vision in the right eye was 20/32.

Intranasal inspection showed a displacement of the left lateral nasal wall toward the septum in the region of the middle turbinate.

The changes revealed by the roentgenograms were diagnostic (figs. 2 and 3).

The Wassermann reaction of the blood was negative. The red blood cell count was 3,430,000, the white blood cell count 8,750 and the hemoglobin value 82 per cent. The urine contained many pus cells.

On July 25, 1936 the frontal sinus was opened by an external approach, with the patient under ether anesthesia. A curvilinear incision was made below the left eyebrow from the external canthus around the inner canthus, with an extension across the bridge of the nose to the opposite brow. A second incision was started at the middle of the left eyebrow and extended upward for 5 cm. The two flaps of skin were dissected back so that the tense, bulging, bluish wall of the mucocele was

exposed. On incision there was an escape of brownish green, glairy, mucoid secretion, viscid enough to be picked up in clumps.

The entire anterior wall of the frontal sinus was absent, the defect measuring 6 by 4 cm. The sinus cavity extended posteriorly about 8 cm into the orbital plate of the frontal bone. The roof of the orbit was absent. The posterior frontal wall and the vault of the ethmoid sinus were intact. No dura was exposed. The mucosa was white, glistening and thin except over the anterior wall, where it was about 8 mm thick. There was no connection with the opposite frontal sinus. The sinus was divided into three compartments by partitions of newly formed, flexible, membranous bone, rising to a height of 2.5 cm as a result of hypertrophy of the usual incomplete septums of the posterior wall. A sound passed through the nasofrontal duct encountered some resistance, apparently due to obstruction.

The mucoid contents of the sinus were emptied, and a portion of the thickened anterior mucosal wall was removed. The nasofrontal passage was enlarged by removal of the infundibular ethmoid cells and a portion of the middle turbinate. A rubber tube was passed into the nose and retained for two weeks.

The postoperative course was uneventful except for some mucoid drainage from the lateral portion of the incision. Sutures were removed in five days. The incision healed with a deep depression. There was some return of light perception after the operation but no actual vision. However, the displaced eye retracted upward until it was only about 0.5 cm below the other. Some movement of the globe and of the upper lid returned. A plastic operation to elevate the eye and fill in the defect was considered. Unfortunately the patient died about six months later, after cholecystectomy.

CASE 2—L. F., man aged 21 years, was seen in my private practice on Jan. 6, 1936. He presented a swelling at the upper inner angle of the right eye. This had been noticed nine years previously, after scarlet fever complicated by sinusitis. It had been aspirated several times but had subsequently refilled. Dull pain was felt occasionally.

There was a small elastic mass above the inner canthus. The palpebral fissure was narrowed and the eye displaced somewhat laterally and downward. Proptosis was not marked. Aspiration yielded an odorless, greenish brown mucoid secretion. The result of a chemical test for cholesterol was positive. On microscopic examination a few epithelial cells and leukocytes were found.

Results of intranasal examination were essentially normal. The nasofrontal duct was probed with a Ritter sound. After penetrating an obstruction, the sound entered the frontal sinus.

Roentgenograms showed haziness of the right frontal sinus, which was regular in outline. There was an oval radiolucent area between the frontal sinuses.

On Feb. 19, 1936 operation by an external approach was done with the region under local anesthesia. There was a large defect in the floor of the sinus, but the anterior wall remained intact. A central cavity about 3 cm in diameter was found communicating with an enlarged frontal sinus on the right and also with the ethmoid labyrinth, due to the absence of most of the lacrimal bone and the lamina papyracea. In the vault of the ethmoid sinus there was an area of exposed dura about 1 by 1.5 cm. The interfrontal septum was absent.

The gelatinous mucoid secretion of the mucocele was evacuated and a portion of the wall excised. Removal of the anterior third of the middle turbinate and some of the anterior ethmoid cells permitted insertion of a tube into the nose through the enlarged nasofrontal duct. The postoperative course was uneventful. One year later the nasofrontal passage was still patent.

DIAGNOSIS

Recognition of a mucocele is based on history, local findings and roentgen appearance. Aspiration is of value but not essential.

Mucoceles must be distinguished from swellings in and adjacent to the orbit and sinuses.

Orbital masses include malignant neoplasms, aneurysms, angiomas, fibromas, lymphoid tumors, enlargements of the lacrimal gland and sac, gummas, osteitis and periostitis.⁶

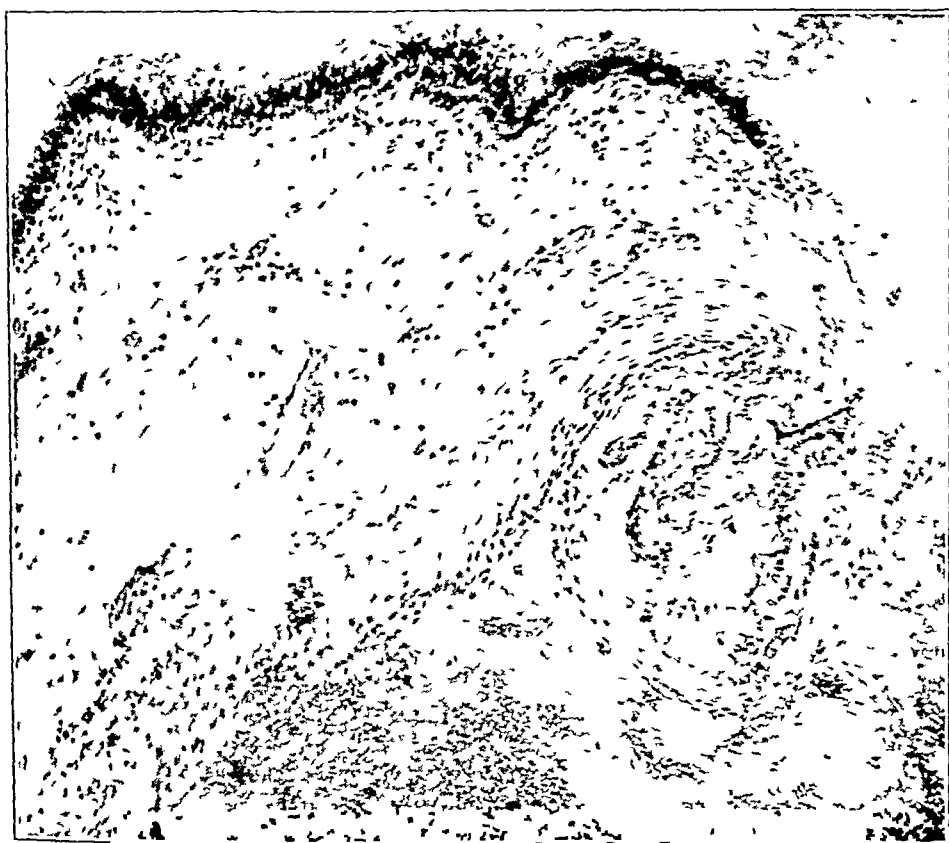


Fig 4 (case 1)—Photomicrograph of hypertrophied wall of the mucocele (hematoxylin and eosin, $\times 150$). There is a great increase of fibrous connective tissue with many new capillaries. The epithelium is generally ciliated, pseudostratified and high columnar. Some areas show a single-layered cuboidal type. The stroma contains extravasated red blood cells, fibroblasts, a moderate number of plasma cells and lymphocytes and polymorphonuclear leukocytes. An occasional mucous gland is present.

Dermoids occur usually at the temporal orbital angle as firm, immobile masses.

⁶ Benedict, W. D. Tumors of the Orbit, in Berens, C. The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 336.

Meningoceles are found earlier in life, they are reduced in size by compression or change in position of the head. Within the sinus osteomas or osteogenetic sarcomas may occur.

PATHOLOGY

The wall of a mucocoele usually shows changes due to pressure. The mucosa is thin, and the columnar epithelium may be flattened, the cilia deficient or absent except for occasional islands. Early, there is dilatation of the mucous glands, followed by atrophy. When a section of the sac wall thickens there are fibrosis, epithelial hyperplasia, capillary proliferation and some infiltration of cells of chronic inflammation (fig. 4).

The sac contains tenacious viscid or gelatinous mucus, yellow or greenish brown, with desquamated epithelial cells, leukocytes, fat cells and, rarely, cholesterol. The bony walls show areas of rarefying osteitis and erosion, but other zones may be stimulated to proliferative changes, associated with formation of new bone around the margins of the sinus.⁷

TREATMENT

Adequate treatment usually requires an external approach through the floor of the frontal sinus, removal of the viscid contents and establishment of a permanent outlet to the nose. In some cases this may be done by the intranasal route. To maintain the nasofrontal passage, a skin graft may be employed. Williams has turned down a flap of mucosa from within the sinus.⁸

Dowman said that his method was to remove the secreting mucosa and to obliterate the sinus cavity.⁹ As a rule, the mucosa may be retained unless grossly hyperplastic.

SUMMARY

Two cases of mucocoele originating in the frontal sinus are presented.

In each case the lesion was successfully managed by an external approach to the frontal sinus and enlargement of the nasofrontal passage.

Noteworthy features of the first case include (1) the giant size of the mucocoele, (2) the secondary pressure, atrophy of the optic nerve, (3) the formation of partial septums of membranous bone within the sinus and (4) the excessive hypertrophy of the sac wall.

In the second case, sinusitis complicating scarlet fever was probably related to the causation. There was dural exposure despite the small external swelling.

NOTE—Since this paper was submitted a third patient has been operated on. This patient, a man 62 years of age, presented clinical and roentgenographic signs of a mucocoele. At operation, via the exter-

7 Logan-Turner, A. Mucocoele of the Accessory Nasal Sinuses, *Edinburgh M J* **64** 396, 1907.

8 Williams, H. L. Mucocoele of the Left Frontal Sinus, *Proc Staff Meet, Mayo Clin* **12** 664 (Oct 20) 1937.

9 Dowman, C. E. Giant Mucocoele of the Frontal Sinus, *J A M A* **81** 1014 (Sept 22) 1923.

nal approach, the sinus was found to be filled with a thin yellowish seropurulent fluid, characteristic of a pyocele. The floor of the sinus and the interfrontal partition were absent. There was exposure of a small area of dura in the posterior wall. The nasofrontal duct was adequately enlarged, and 50 mg of radium was inserted for a three hour period. At this writing a no. 7 Ritter sound can be passed through the duct without difficulty. However, it is only six weeks since the operation.

Williams and Fricke¹⁰ have devised this technic for the preservation of the patency of the duct after external frontoethmoidal sinusectomy. The rationale of the procedure depends on the effect of irradiation in inhibiting the excessive growth of connective tissue and thus obviating subsequent scar formation and stenosis. They reported excellent results. In 16 operations followed by the use of radium there was partial closure of the frontonasal duct in 1 case, and the percentage of failure was 6. In contrast, in 47 operations following which radium was not used, failure due to closure of the frontonasal opening occurred in 19 per cent of the cases.

25 East Washington Street

10 Williams, H. L., and Fricke, R. E. Use of Radium in Maintaining Patent Frontonasal Opening in External Operations on the Fronto-Ethmoid Group of Sinuses. A Preliminary Report, *Ann Otol, Rhin & Laryng* **48** 412 (June) 1939.

THROMBOSIS OF THE LATERAL SINUS AND ABSCESS OF THE TEMPORAL LOBE DUE TO BACILLUS PROTEUS

ROBERT M. DEARMIN, M.D., AND J. LAWRENCE SIMS, M.D., INDIANAPOLIS

This case of mastoiditis due to *Bacillus proteus* is reported because of the many complications and of the fact that recovery occurred. Recently Gerzog¹ published an interesting resume concerning such infections. He emphasized the extensive destruction of dura. The present report confirms previous statements as to the extreme morbidity resulting from this organism's activity. In 1936 McGovern² emphasized the seriousness of mastoiditis due to *B. proteus* and reported 2 cases. At operation, a foul, destructive process of the sinus wall was disclosed in both of these cases. In both death occurred, autopsy in 1 case showing multiple lung infarcts, abscesses, empyema and lobular pneumonia. In the other, a case similar to those of Gerzog, an extensive destructive process involving the dura was revealed. In this case death was apparently due to the associated septicemia.

Salient points regarding the otogenic behavior of *B. proteus* warrant reaffirmation, namely: 1. The site is usually a chronically discharging ear, the bacillus acting as a secondary invader in most instances. 2. The vasculature of the field appears extremely inviting to the organism, with the result that perisinus abscesses and lateral sinus thromboses are frequent. 3. The progression in these cases is woefully extensive, meningitis and abscess of the brain thus being produced at times. Although the case to be reported here demonstrated all features just named, it will be seen that the disease progressed slowly, fortunately however, complete recovery was achieved.

REPORT OF A CASE

J. M., a man aged 23, entered the Robert Long Hospital on Aug. 10, 1939 as an emergency patient because of irrationality, severe bursting headaches, sepsis and intermittent coma. During the few days just prior to admission he required drastic stimulants on several occasions.

History—The patient's family disclosed that he had had discharging ears since he was 6 years of age. A simple mastoidectomy on the left had been performed at the age of 7 years. Since then, however, both ears had drained constantly with resultant erosion of both drums. He wore a bone conduction hearing aid. The past and the family history were otherwise noninformative.

From the Department of Otolaryngology, Indiana University School of Medicine.

1 Gerzog, B. G. *Bacillus Proteus* in Otogenic Infections, Secondary Mastoiditis, Thrombosis of the Lateral Sinus and Bacteremia, *Arch. Otolaryng.* **30** 275-279 (Aug.) 1939.

2 McGovern, F. H. Fatal Otogenic Infection with *Bacillus Proteus*, *Arch. Otolaryng.* **24** 618-621 (Nov.) 1936.

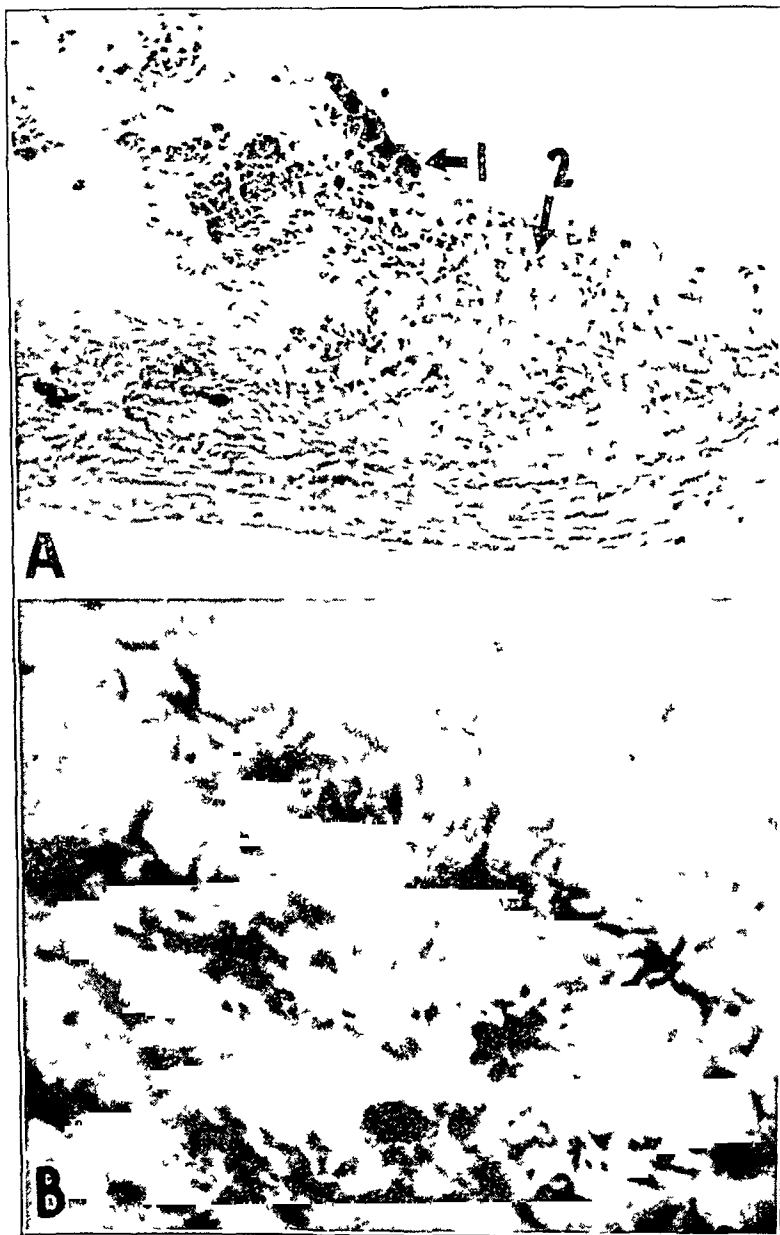
Present Illness—The onset of the present illness was approximately one and a half months before his admission to the hospital and was characterized by (1) severe chills, (2) fever, (3) headache, for the most part frontal and occipital, (4) swelling of and about the left ear and (5) occasional delirium. He was taken to the Mary Sherman Hospital in Sullivan, Ind., on June 28, 1939, where owing to the edematous swelling of the left auricle and to the accompanying clinical picture a diagnosis of erysipelas was made. Gradual improvement was noted to result from the use of sulfanilamide, application of packs to the left ear and general supportive measures. While he was there however, the left ear drained intermittently and also began to discharge through the old mastoidectomy incision. Since eventually he was able to sit up and take nourishment, he was returned to his home on July 28, 1939. An acute exacerbation of the aforementioned symptoms prompted his admission to the Indiana University Hospitals as an emergency patient on Aug. 10, 1939.

Physical Examination on Admission—The patient was moribund, emaciated and stuporous. Purulent, foul drainage exuded from the left ear and through the old mastoidectomy incision. The right middle ear also showed considerable erosion and contained a moderate amount of chronic foul drainage. The eyes reacted sluggishly to light and in accommodation. Bilateral papilledema, lateral nystagmus and a positive Kernig sign in the neck and legs were found. A definite facial weakness was present on the left. The pulse rate ranged between 40 and 50. When aroused, he demonstrated obvious anomia (history revealed him to be right handed).

Laboratory Findings on Admission—The leukocyte count was 12,500, the erythrocyte count 3,400,000 and the value for hemoglobin 66 per cent. Spinal puncture revealed a pressure of 30 mm. of mercury, together with a white cell count of 648, a trace of globulin, a sugar content of 44 mg. per hundred cubic centimeters of fluid and a protein value of 105 mg. per hundred cubic centimeters. The Tobey-Ayer test demonstrated no rise on the left and a rise of 8 mm. of mercury on the right. Culture of spinal fluid revealed no organism.

Treatment and Progress—On the assumption that the patient had secondary recurrent mastoiditis complicated by lateral sinus thrombosis, septicemia, serous meningitis and abscess of the temporal lobe, it was decided to operate immediately. Through a T-shaped postauricular incision the cortex was exposed extensively. Considerable sclerosis was found throughout the mastoid cavity. The antrum was large, containing cholesteatoma and foul-smelling pus. The posterior canal wall was taken down, the operation thus being converted into a radical mastoidectomy. Both the middle and the posterior fossa were exposed widely. The lateral sinus was found to be completely necrosed and at some points apparently organizing. Free bleeding could be obtained only at the torcular end. This was controlled by means of cotton pledgets used as packing. The dura of this region appeared gray, being covered by unhealthy granulations. No effort was made to obtain bleeding from the distal end of the sinus. The dura of the middle fossa was comparatively normal in appearance, but because of the aphasia and partial paralysis of the facial nerve on the left side, this dura was nicked. At a depth of 3 cm. a large abscess of the temporal lobe was found, and approximately 30 cc. of thin, foul-smelling pus was released. No stalk of attachment for the abscess could be found. A Pezzer self-retaining catheter was inserted as a drain. The wound was packed wide open with iodoform gauze.

Postoperatively the patient showed slow but progressive recovery. He received intravenous fluids, irrigations of the brain abscess as indicated and transfusions of large amounts of blood (on the first, second, third, sixteenth and twenty-second hospital days). The mind began to clear within a few days after the operation. The



Photomicrographs of a section of a diseased thrombus. *A*, a section through a representative portion of the thrombus, shows at 1 a densely infected area and at 2 beginning organization of the thrombus. *B*, an enlargement of an area near 1 in *A*, shows a mass of *B. proteus*.

packing was removed from the torcular end of the sinus on the fourth postoperative day. At times the patient would become nauseated and complain of severe head-

ache This condition was usually relieved by irrigations of the abscess cavity The anemia subsequently disappeared The mushroom-tipped catheter was replaced by a plain one on Sept 19, 1939 This was gradually shortened as the abscess filled in The patient was discharged in good condition on Nov 4, 1939 He was seen subsequently in the outpatient clinic on Oct 1, 1940 He is apparently cured

Laboratory Findings After Operation—The leukocyte and the differential count became normal Reactions to Kline and Mazzini tests of the blood were normal Cultures of material obtained from both the mastoid process and the abscess of the temporal lobe showed *B. proteus* Microscopic examination of a section of the thrombus demonstrated a marked inflammatory reaction and necrosis as well as some areas of clot showing partial organization, as illustrated in the accompanying photomicrographs

SUMMARY

Important considerations concerning otogenic infections by *B. proteus* are outlined briefly, with particular emphasis on the associated morbidity

A case is reported in which recovery occurred even though the mastoiditis was complicated by lateral sinus thrombosis and abscess of the temporal lobe

The successful termination is thought to be due to the removal of the infected tissue, to the complete open drainage of the involved field and to the supportive care given the patient postoperatively

Clinical Notes; New Instruments and Technics

NEW INSTRUMENTS FOR USE IN RHINOPLASTIC SURGERY

JOHN A. CINELLI, M.D., NEW YORK

Assistant Surgeon, Bellevue Hospital

The following new instruments have been devised to aid the rhinoplastic surgeon in obtaining better results with the least possible trauma and in the shortest time. They are also intended to solve some difficult problems with which the surgeon may be confronted. They are (1) a perforated saw guide, (2) a periosteal elevator and saw director, (3) a nasal chisel, (4) an alar forceps and (5) a nasal saw director.

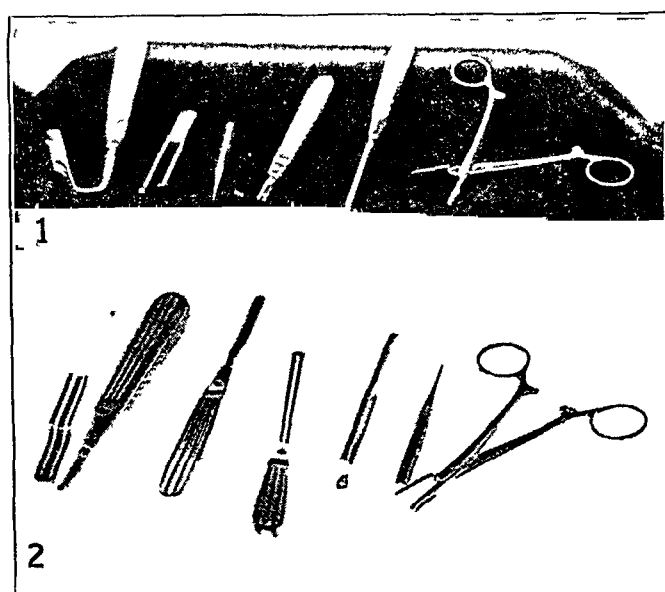


Fig 1—(From left to right), 1, nasal saw director, nasal chisel, sharp-pointed steel puncture rod (used with nasal chisel), perforated saw guide, periosteal elevator and saw director, alar forceps 2 (from left to right), nasal saw director, periosteal elevator and saw director, perforated saw guide, nasal chisel, sharp-pointed steel puncture rod (used with nasal chisel), alar forceps

The perforated saw guide (fig 2) is intended for use only by the beginner who experiences some difficulty in securing the saw in the desired position along the nasofacial angle of the nose. When the saw guide is placed at the nasal-facial angle or at the internasal suture line the saw is permitted to enter the perforation in the instrument. The guide is then held securely with the left hand, and with the right hand the surgeon can saw through the bone with either a straight or a right-angled saw. This instrument assures steadiness, which is often lacking in a beginner.

The purpose of the periosteal elevator and saw director (fig 3) is twofold. First, it elevates the periosteum at the nasofacial angle, and, second, it guides

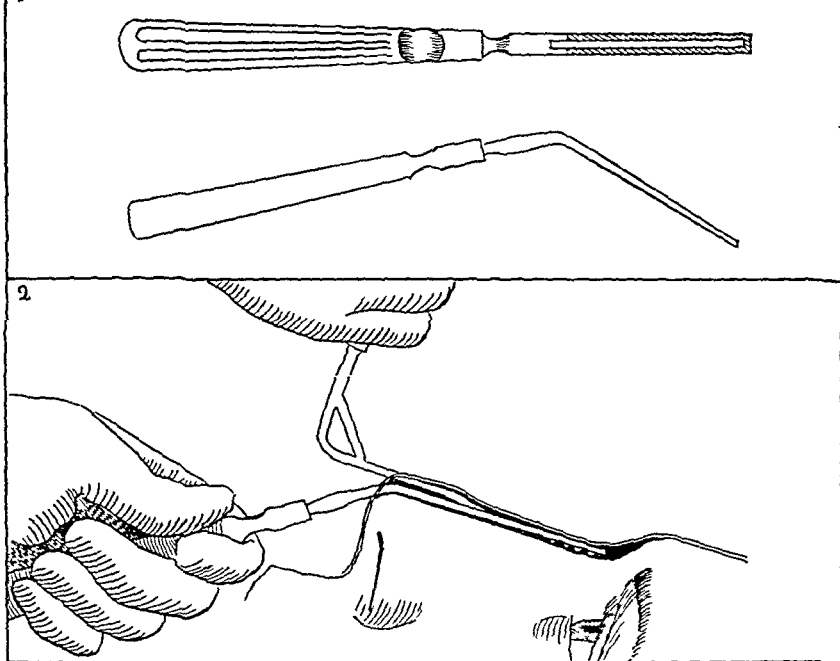


Fig 2—A perforated saw guide 1, top view and side view 2, the instrument in position for use

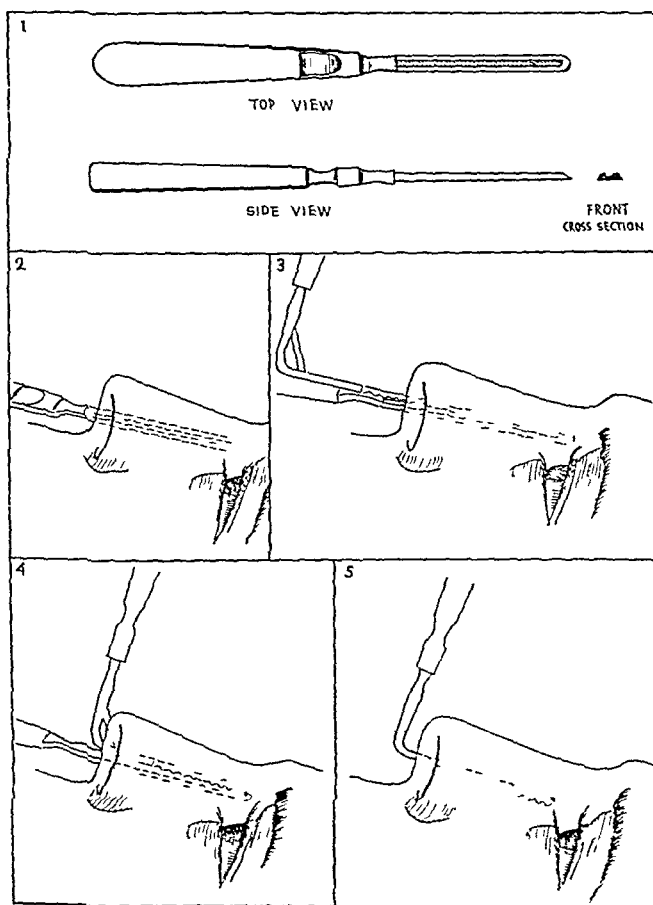


Fig 3—1, top view and side view of the periosteal elevator and saw director 2, 3, 4, 5, steps in the use of the instrument

the saw into its proper place at this angle. After the initial incision is made at the piriform aperture of the nose, the instrument is inserted and the periosteum is gently lifted. Then, without removal of the instrument, the saw is placed in the grooved shaft and gently pushed upward to the frontonasal suture line. The instrument is then taken out by raising the saw off the grooved shaft. By the use of this instrument the operator avoids the usual hindrance encountered when the teeth of the saw come in contact with the nasal tissues. Frequently the surgeon exerts a great deal of pressure in order to insert the saw in the proper place. This invariably causes a great deal of trauma and some delay. It is obvious, then, that this instrument saves time and prevents unnecessary trauma.

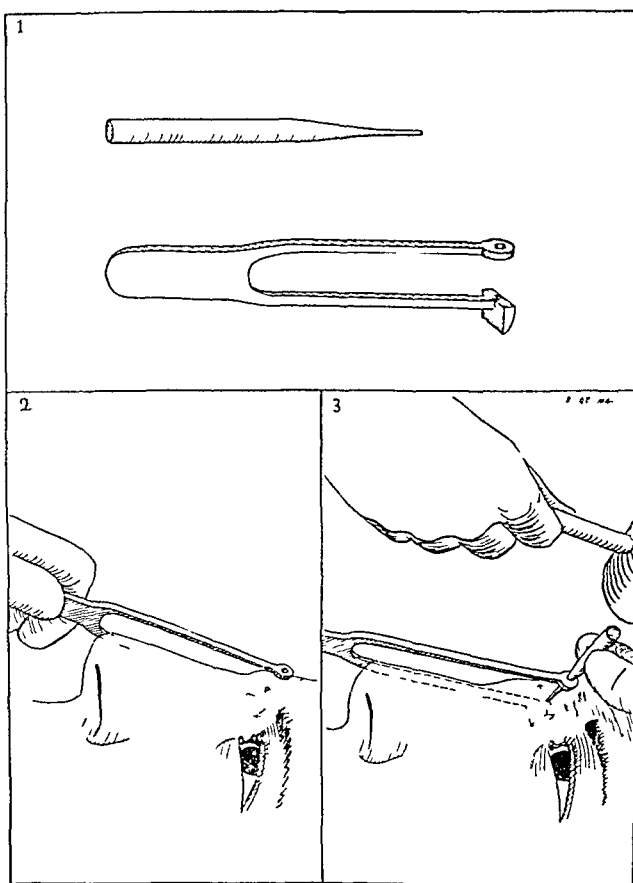


FIG 4—1, sharp-pointed steel puncture rod and nasal chisel. 2 and 3, steps in the use of the instruments.

There are times when the rhinoplastic surgeon is confronted with the problem of how to fracture the frontonasal suture line after digital pressure has failed. All rhinoplastic surgeons know that when the hump is removed and the base of the nose is fractured through, the frontonasal suture line must be broken through in order to close the gap created by the removal of the hump to produce a narrow bridge. Some surgeons cut through the skin at a point directly overlying the frontonasal suture line. Other operators use the eyebrows as a means of approach, i. e., they make an incision in the corresponding eyebrow and insert a chisel through it down to the desired suture line. The objections to these methods are that they leave a visible scar, in the first case, and cause much trauma, in the second. The

new nasal chisel (fig 4) is inserted beneath the skin and directly in contact with the frontonasal suture line. The outer arm is perforated at its end in order to permit a sharp-pointed steel puncture rod to enter. A dotlike nick is made through the skin. The point of the puncture rod is then made to rest securely in the depressed area of the chisel. Several blows on this rod usually suffice to break the fronto-nasal suture line. The dotlike nick need not be closed with any suture material. As one can see in figure 4, 2, the perforation of the end of the outer part of the arm is perpendicular to the center (depressed area) of the chisel, the lower part of the arm

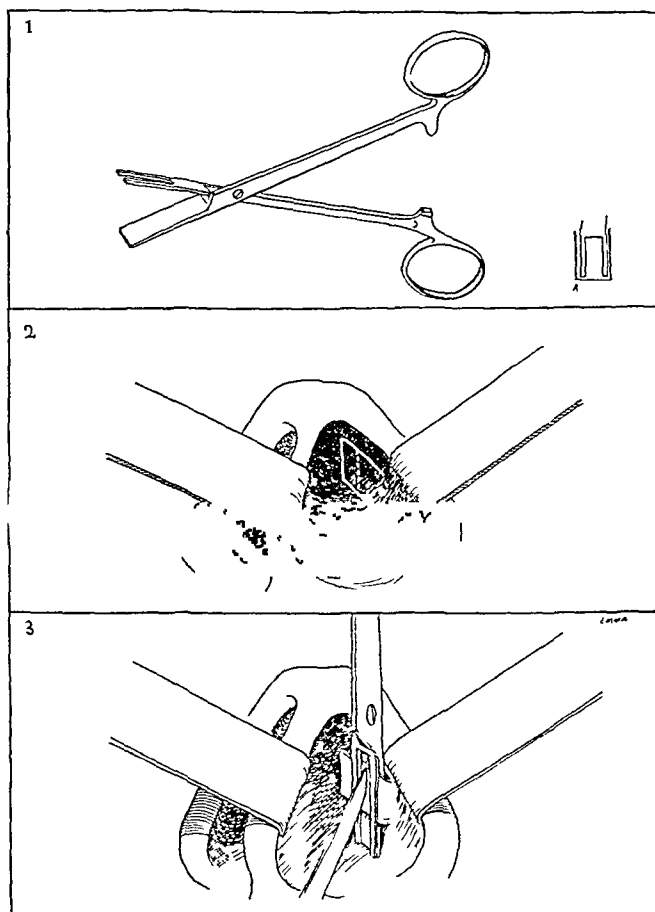


Fig 5—1, alar forceps 2, an area where the instrument is to be used 3 the instrument in position for use

The alar forceps (fig 5) is useful in those cases in which the alar pedicle flap operation is utilized in order to reduce a wide or bulbous nasal tip. After the lateral crus is completely separated from the overlying skin, the alar forceps grasps this cartilage in such a way that the inner margin of the forceps coincides with the angle of the alar cartilages, i e., the point where the lateral crus joins the medial crus. The surgeon can now excise a segment of the cartilage at three different points, A, B and C (fig 5, 3), depending on the amount of reduction desired. At no point selected can the blade cut through the skin, as the flat arm of the instrument always comes in contact with the blade once it has pierced the cartilage. Advantages in the use of this instrument are (1) it prevents the

unnecessary trauma caused by a mouse-toothed forceps, which constantly slips and tears the delicate mucous membrane, (2) it holds the cartilage in any desired position, (3) it gives better exposure of the alar cartilage, (4) it saves time, and (5) it enables the surgeon to estimate the amount of cartilage to be removed on the opposite side

It has been my observation that some surgeons experience a great deal of difficulty in determining the exact position of the saw when the nasal bones are to be sawed through on either side of the perpendicular plate of the ethmoid. The use of the nasal saw director is indicated only in those cases in which there is a broad bridge without any nasal hump. The end of the nasal saw director (fig 6)

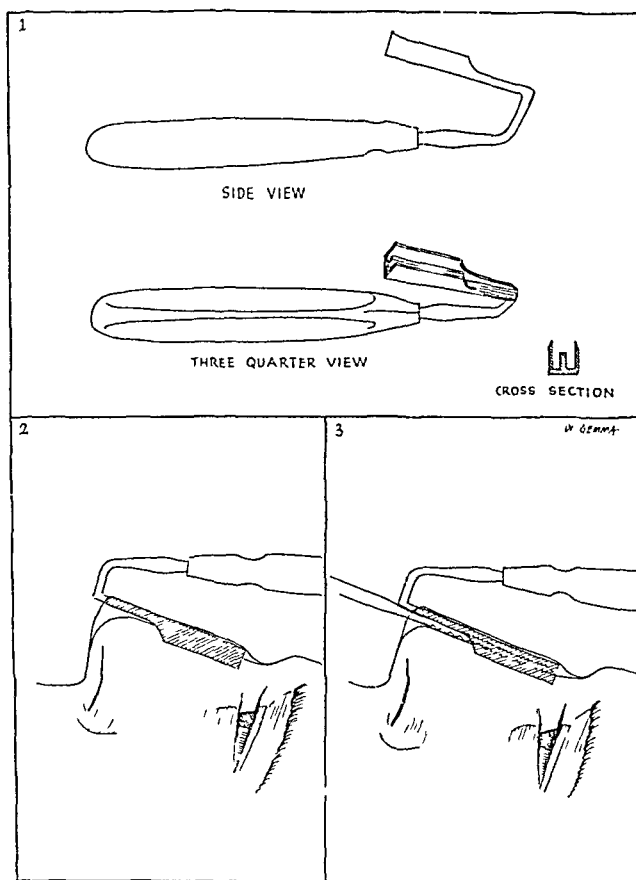


Fig 6—1, side view, three quarter view and cross section of the nasal saw director 2 and 3, steps in the use of the instrument

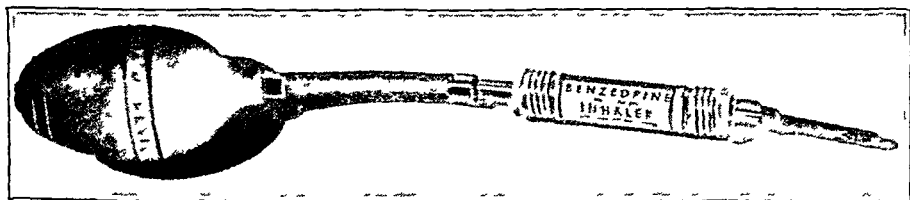
which rests on the nasal bones is grooved on either side, so as to permit the passage of a right nasal saw in the right groove and a left nasal saw in the left groove. The instrument is held securely in place by grasping the handle with the left hand and resting the hand on the forehead. The saw is permitted to enter the corresponding groove. The surgeon can then saw through the medial border of the nasal bone with the greatest ease and security. A straight cleancut separation is thereby obtained. This instrument enables the surgeon to avoid the irregular saw lines ordinarily obtained. It prevents trauma to the overlying skin, which is held against the saw in order to keep it in the direction desired. This instrument also saves considerable time by giving the operator confidence and security in its handling.

A TECHNIC FOR INSUFFLATING BENZEDRINE VAPOR IN CASES OF SINUSITIS IN INFANTS

HENRY A MILLER, M D, PHILADELPHIA

A study of 43 cases of anterior ethmoiditis in infants under 2 years of age at the Children's Hospital in Philadelphia revealed that the most characteristic symptom was marked inflammation of the middle turbinate. The nasal mucosa was examined with a 5 mm speculum on an electric otoscope.

The following technic was evolved for symptomatic treatment. A benzedrine inhaler, fitted with adapters supplied by the manufacturer, was attached to an insufflating bulb, and the male adapter was inserted into a rubber nozzle made from a no. 12 French catheter. The nozzle was introduced into the nostril, and two insufflations were given on each side, after which the nares were covered with



Direct benzedrine-insufflative apparatus for infants

gauze in order to prevent too rapid dissipation of the vapor. Treatments were given twice daily. When necessary, nasal discharge was removed by mass suction with a hand bulb, as described by Campbell¹.

RESULTS

It was apparent that the treatments were beneficial in that they improved respiration. There was also a definite clinical impression that the course of the infection was shortened in most cases, in proportion to the symptomatic relief obtained.

In the most severe acute infections it was not possible to prevent the development of otitis media, which sometimes occurred within a few hours after admission. The treatment failed in 20 per cent of the cases. These were characterized by persistent inflammation of the middle turbinate which did not subside with the other symptoms. In most of these cases there were subsequent exacerbations, and the condition was classed as chronic sinusitis. It may be concluded that the treatment is best adapted to acute attacks.

There were no undesirable reactions.

¹ Campbell, E H. Association of Acute Sinusitis and Otitis Media in Infants and Children, Arch Otolaryng 16 829-845 (Dec) 1932

INTRAVENOUS INJECTIONS THROUGH THE VENOUS PLEXUS OF THE NOSE

Preliminary Report

H P SCHUGT, M D, New York

The veins of the body surface, mainly the veins of the arm, leg, neck and head, are commonly used for intravenous therapy. It is, however, not generally known that the venous system of the interior of the nose can be used for the same purpose.

The inferior turbinate of the nose contains numerous thin-walled venous channels between its surface and the bony structure of the turbinal body. These vessels are known to be capable of being enormously distended with blood. F Polte¹ for the first time employed this area of the nose for intravenous injections of arsphenamine and reported his experiences in a small number of cases. Early in 1923 I injected arsphenamine through the nose without difficulty and without seeing any harmful local after-effects in the nose. This method attracted little attention until O Six² took up the question again and worked out the technic in the treatment of 20 patients, also using arsphenamine for injections. Since then nothing, as far as I know, has been published on the subject. Certain objections may be made to the method by those who doubt the possibility that the general venous system of the body can be reached through the nose in the same way as is possible through the veins of the body surface, such as the cubital vein. I have used the nasal method in the treatment of a larger group of patients during the last four years and think it worth while to report my experiences. The main object in employing this method was to determine whether the injected fluid reached the general circulatory system in a similar manner and in about the same time through the veins of the nose as it would when injected through the cubital vein. This, I thought, could be ascertained best if a preparation was used that would create a general reaction in the body either during or immediately after the process of injection. I found calcium gluconate an especially useful drug for this purpose, for it is known to cause a sensation of heat in the body as soon as it is absorbed in large quantities. I have injected this preparation through the turbinal body of 50 patients with allergic rhinitis. The patients indicated that they felt a sensation of heat while the calcium was being injected. The majority noticed the heat first in the back and in the legs and spreading thereafter over the entire body, so that I had to assume that the fluid did not remain in the nasal tissues but was immediately absorbed into the general venous system in about the same time as it would have taken when given through the cubital vein. The technic is very simple and may be used by anybody who is familiar with the anatomy of the nasal structures. A head mirror and a speculum are the necessary instruments, the inferior turbinate is brought into view with the speculum, and the needle (2 inches [5.08 cm] long, attached to the syringe) is inserted into the anterior tip of the turbinate far enough to reach the bony part of the turbinate. The needle is then drawn back a little to avoid injections under the periosteum of the turbinate. The latter procedure is important in order to avoid bony necrosis and to stay within the vascular system of the turbinal body. It is not possible

1 Polte, F. Erfahrungen bei Injektionen von Salvarsan in die Nasenmuscheln, *Ztschr f Hals-, Nasen- u Ohrenh* **2** 281-282, 1922

2 Six, O. Ueber eine bequeme Art der Salvarsoninjektion in die Nasenmuscheln, *Beitr z Anat, Physiol, Path u Therap d Ohres* **23** 93-97, 1926

and it proved unnecessary to withdraw blood from the turbinate into the syringe, as is usually done before making an injection into the cubital vein. The initial amount of the preparation is injected with gentle pressure, to assure its smooth flow through the turbinate. Once this is established, the remainder of the preparation can be injected almost as fast as it is through the cubital vein or any other vein of the body surface. There is no noticeable distention of the turbinal body during the injection. The procedure is generally painless, local anesthesia of the turbinate is just as unnecessary as it is when injections are made elsewhere in the body. Cocaine is not to be used, because it contracts the blood vessels and thereby interferes with the injections.

I may add that after the injection is completed and the needle removed there will be slight bleeding from the point of puncture. To counteract this, I apply a piece of cotton soaked in a solution of epinephrine hydrochloride (1:1,000) to the injected turbinate after removing the needle. This will cause contraction of the part of the turbinate where the injection was made.

The question has been brought up whether necrosis may occur. I have never seen it, neither did Polte,¹ who first employed this method, report any.

Six² described a case in which part of the inferior turbinate sloughed out. This, I am sure, will happen only with a faulty technic, just as it is occasionally seen after an injection through the cubital vein.

The ages of my patients varied between 18 and 70 years. The oldest patient received sodium gold thiosulfate (10 cc) for arthritis without any local reaction in the nose. I have never noticed a secondary atrophy of the turbinal body, even after repeated injections. The largest quantity so far injected has been 20 cc. I have not had the opportunity as yet to use this method in the treatment of children.

For obvious reasons it is contraindicated in the treatment of patients with atrophy of the nasal mucosa (ozena).

I realize that this method of intravenous therapy cannot replace the commonly used method of injecting through the veins of the arm, nevertheless, it seems to be of more than theoretic interest to know that the nasal way may be considered desirable in cases in which, for some reason or other, the former method presents difficulties.

SUMMARY

The venous system of the inferior turbinate of the nose can be used for intravenous injections. The technic and the experiences of the author are described in detail.

INTRANASAL LIGATION FOR EPISTAXIS

LLOYD K. ROSENVOLD, M.D., GLENDALE, CALIF.

As is well known, epistaxis frequently occurs from dilated blood vessels (Kiesselbach's plexus) near the anterior part (Little's area) of the nasal septum. Often this plexus of vessels can be seen to communicate with one larger vessel, which crosses the floor of the nasal vestibule in a transverse direction. Usually these vessels are venous, but sometimes they appear to be arterial and to represent septal branches of the superior coronary artery. Study of cadavers reveals the origin of the septal arteries.

Cauterization (chemical, thermal, electrical) has been commonly used to ablate these dilated vessels from the septum. After cauterization there sometimes is

From the Department of Otolaryngology, College of Medical Evangelists

additional bleeding when the crust falls off, and in the end permanent mucosal crusting is occasionally seen. Subperichondrial elevation of the bleeding areas has given good results, but this is rather formidable compared to the simple procedure to be described here. Three years ago I conceived the idea of ligating the large connecting vessel in cases of epistaxis from dilated vessels on the septum in which this large vessel can be seen entering the floor of the vestibule.

PROCEDURE

The mucosa of the anterior part of the septum is cocaineized. The cutaneous floor of the vestibule is anesthetized by the injection of 1 to 2 cc of a 1 per cent solution of procaine hydrochloride. A deep suture of no. 00 chromic catgut is then placed in the floor of the vestibule. This passes deep to the blood vessel traversing the area. A good square knot is tied.

The suturing can be accomplished by the use of (1) an angular Yankauer nasal needle, (2) a small half-curved needle or (3) a no. 18 hypodermic needle, through which the suture will pass. Tying of the knot is facilitated by the use of a forceps.

No special postoperative care is necessary. The patient is instructed not to disturb the suture and to use petrolatum or cold cream in the naris if irritation is too great.

I have personally used this method in 13 cases with essentially good results. In 2 other cases, in which a vessel was not seen in the vestibular floor but the ligation was done empirically, the patients were not benefited. Patients that had been bleeding practically daily or weekly for weeks, months or many years had no more bleeding. No untoward results were observed in this series. Often one can actually notice the diminution in the size of the septal blood vessels following this procedure. Individual case reports will be omitted, to conserve space.

I have found no reports of this procedure in the literature. It is not a cure-all but is merely recommended as a mode of treatment that has proved useful in selected cases both in my practice and in that of several colleagues who have used it on a number of patients.

1509 East Wilson

Correspondence

"THE PHYSICAL STANDARDS UNDER SELECTIVE SERVICE"

To the Editor —Dr George B Wood has drawn my attention to the publication in *The Journal of the American Medical Association* of the article "Physical Standards Under Selective Service" (Nov 2, 1940), in which appears a reference to the determination of deafness malingering by the use of two tests—the Chimani-Moos test and the Erhard test. Neither Dr Wood nor I had recalled these tests, and it occurs to me that many other experienced otologists are ignorant of them. It would be advisable, then, to publish a description of the tests and, at the same time, to state that it seems strange that the Stenger test (which has long been recognized as the most familiar and efficient test) has been omitted by the military authorities.

These tests are described by Wendell C Phillips in "Diseases of the Ear, Nose and Throat" (F A Davis Company, 1919) as follows:

"CHIMANI-MOOS TEST —A large-sized tuning fork, C2, is held alternately at an equal distance from each ear. In this manner it becomes self-evident that the tone is heard better in the ear which is claimed to be sound. The vibrating tuning fork is then placed on the median line of the vertex, or against the incisor teeth, and the patient asked to indicate in which ear the tone is better perceived. The patient with true aural disease affecting the sound-conducting apparatus will state without hesitation that he hears the tone much louder in the diseased ear, while the malingerer, after hesitating for a moment, inasmuch as he is really unable to distinguish any difference of perception in the two ears, thinks that he is answering correctly by stating that he hears the tone in the normal ear. If, then, the external meatus of the normal ear is tightly closed and the vibrating fork is again placed on the vertex or incisor teeth, the individual, if really deaf, will now say that he hears the tone better in the closed normal ear, or, he may no longer be able to distinguish on which side he perceives the tone. The malingerer, with the normal ear tightly closed will state that he does not hear the tuning fork placed upon the vertex or incisor teeth at all.

"ERHARD'S TEST —If the external meatus of a normal ear is tightly packed it will still conduct the sound waves to a limited extent, a loud ticking watch being heard at a distance of 2 or 3 m. Erhard places the malingerer in the middle of a large room, closes the ear which is said to be deaf, and then brings a loud ticking watch gradually toward the normal ear and orders the patient to count the beats. The normal ear is then tightly closed and the supposed diseased ear examined. If the malingerer claims that he does not hear the watch-tick at a distance of 1 or 2 m (the distance at which the tick should be heard in the closed normal ear) simulating should be suspected. (A proper criticism of the Erhard Test is that it deals entirely with malingering of hearing by the good ear, and does not prove hearing in the ear claimed to be deaf.)"

In addition to submitting this complaint, I should like to request elucidation of the instructions: "Acuity of hearing will be determined by the low conversational voice test and by the audiometer when indicated." No mention is made as to how to determine when the use of the audiometer is indicated.

DOUGLAS MACFARLAN, M D, Philadelphia

Abstracts from Current Literature

Ear

CEREBRAL EDEMA AS A CAUSE OF INTRACRANIAL HYPERTENSION OF OTITIC ORIGIN NORMAN A LEVY, *Ann Otol, Rhin & Laryng* 48 999 (Dec) 1939

The author reports a case of persistent cerebral edema developed in the course of suppurative otitis media, which he believed might be due to venous stasis caused by infection of the dural sinuses. He feels that in many cases increased intracranial tension in the course of otitic infections may be due to cerebral edema. He discusses the venous circulation in the cranial cavity and the manner in which it may become congested or a congestion may be increased by various factors. The anatomic variations in the lateral sinuses of the two sides, variations in the size of the mastoid veins, the role played by lack of valves, the tortuosity and the negative pressure in the venous sinuses are discussed, and the part these may play in the development of increased intracranial pressure in the presence of sinus thrombosis, partial or complete, or even in the absence of involvement of the sinuses. Change in the venous pressure, either generalized or confined to the head, is accompanied by similar changes in the cerebrospinal fluid. He says that chronic localized adhesive leptomeningitis may cause a damming of the cerebrospinal fluid and a dilatation of the ventricular system. Such chronic adhesive arachnoiditis should be carefully differentiated from intracranial hypotension caused by cerebral edema, as the treatments are usually different. M V MILLER, Philadelphia

STUDIES IN LABYRINTHINE FENESTRATION TO IMPROVE HEARING (A PRELIMINARY REPORT) SAMUEL J KOPETZKY, *Laryngoscope* 49 1064 (Nov) 1939

Kopetzky selects 8 cases of labyrinthine fenestration for critical study of the function of the ear in the light of his results of fistulization, he suggests that the results warrant a reexamination of the theories of hearing.

He made the following observations: 1 After the removal of a cholesteatoma that has eroded a semicircular canal, the fistula may persist without improvement of hearing. 2 A fistula may close but the improved hearing level be maintained. 3 Improvement of hearing in the opposite ear, unoperated on, may occur and follow the improvement of the ear which has been operated on. 4 Fenestration is applicable to ears that have previously had radical mastoidectomies, a fact which shows that the presence of tympanic structures is unessential. 5 Fenestration may be accomplished through the conventional postauricular mastoid exenteration without disturbing the middle ear or the epitympanic space. 6 A permanently open fenestrum is not the sole factor in establishing and maintaining better acuity in hearing. 7 The necessity for retaining the incus always and the absolute need of a flap for improvement of hearing are questioned.

One patient who had surgical destruction of the membranous horizontal semicircular canal with no subsequent infection suffered no loss of hearing. Kopetzky's best results were obtained with a fenestration of from 1 to 3 mm in length. He observed instances of even a persistently open fistula, in which the hearing gradually diminished and the initial gain was lost. The improvement of hearing in the ear on which operation was not done suggests reexamination of fundamentals of hearing.

Wood, Newark, N J

THE EXPERIMENTAL PRODUCTION OF DEAFNESS IN YOUNG ANIMALS BY DIET EDWARD MELLANBY, *Laryngoscope* 49 1090 (Nov) 1939

Mellanby produced in young dogs by an experimental diet a pathologic condition of the labyrinthine capsule, both of the nerve supply and of the bone itself.

The diet was deficient in vitamin A and carotene, it included much cereal and all other food values

Litters of puppies 7 to 10 weeks old were started on the experimental diet deficient in vitamin A. Usually the behavior of the animals became abnormal after two to four months of such feeding, with great changes after four months. The dietetic periods were from four to ten months. A total of 51 labyrinths from 44 dogs were examined. Serial sections of 16 of these from 12 animals were cut, stained and examined. The histologic technic of the Ferens Institute for the Study of Otology was used with modifications. Apart from the specific effects produced by the vitamin A deficiency the health of the animals was usually fairly good, with steady gain in weight. Mellanby gives, as follows, the most obvious pathologic changes found in the labyrinths of these young dogs: "*a* nerve degeneration, more especially of the cochlear neurones, *b* new bony growth in the modiolus, *c* overgrowth of the internal periosteal layer of the capsule, *d* serous labyrinthitis, *e* degenerative changes of the organ of Corti and sensory epithelium of the semicircular canals." The new bone laid down was of periosteal origin and appeared constantly in two places, (1) in or near the modiolus and (2) round the internal auditory meatus. This new bone pressed on and elongated the nerves as they left the cochlea and vestibule. The degeneration of the eighth nerve, especially the cochlear neurons, appeared to be due to mechanical interference produced by bony overgrowth. Where bony overgrowth and nerve degeneration were advanced, serous labyrinthitis was always found.

Wood, Newark, N. J.

THE PATHOGENESIS OF OTOSCLEROSIS. WILLIAM SPARER, *Laryngoscope* **49** 1199 (Dec.) 1939

After reviewing the theories of the pathogenesis of otosclerosis, Spierer suggests that the condition is the result of a vasomotor imbalance of the blood vessels of the middle ear controlled through the fibers of the tympanic plexus and that this in turn is influenced through the sphenopalatine ganglion by a pathologic condition of the nasal sinuses. He explains the histopathologic changes of otosclerosis on the same basis as the bone changes in nasal sinusitis, ascribing them, that is, to alteration in local circulation secondary to vasomotor imbalance in the sympatho-parasympathetic nerves. For patients with a family history of progressive deafness, he suggests as prevention and treatment of otosclerosis: (1) detection and eradication of nasal disease, (2) examination by serial audiograms at regular frequent intervals to detect the first decrease of hearing, and (3) at the first observation of loss of hearing, injection of alcohol into the sphenopalatine ganglion to disrupt efferent irritating impulses before they produce chronic changes in the blood vessels of the middle ear.

Wood, Newark, N. J.

ANATOMY AND TOPOGRAPHY OF THE SENSORY ELEMENTS OF THE VESTIBULAR LABYRINTH. A. VAN EGMOND, *Oto-rhino-laryng internat* **24** 46 (Feb.) 1940

The sensory epithelium of the cristae and maculas rests on a thin fibrous membrane, the basilar membrane. Surmounting the cristae and the maculas are the cupula and the otolithic membrane, respectively, sensory threads ramify in the intervening spaces. The cupula is a transparent gelatinous mass. The otolithic membrane encloses chalk crystals of varied sizes. Wittmaack has demonstrated that the cupula contracts under the influence of acids, by excitation from cold water and from the anode, alkalis, warm water and the cathode cause it to expand. His theory of turgor is built on these observations. In the living state the cupula fills almost completely the space between the crista and the roof of the ampulla. In man the proportion between the size of the anterior and posterior planes of the utricular macula is $1 \frac{2}{4}$. The macula of the saccule presents three planes, dorsal, anterior and principal, which are related in size to each other in the proportion of 1 1 2 (measurements on rabbits). The epithelium of the cristae and maculas consists of hair cells, supporting cells and marginal cells. The

hair cells have the shape of a bottle, the protoplasm surrounding the nucleus is clear and the nucleus is situated in the lower part, particles of fat and lipoids are found at the periphery. The free surface of the hair cells is covered by a cuticular plate, here a diplosome is situated which gives rise to a very slender elastic thread. Also originating in the cuticular plate, but independent of the elastic threads, are the sensory threads, composed of a number of hairs bound together by a homogeneous substance. The supporting cells lie between the sensory cells, and there is no protoplasmic connection between them. The length of the supporting cells is almost twice that of the hair cells. The nucleus lies in the lower part, the protoplasm is traversed longitudinally by fibers called *tonofibrilles*. Werner has observed regional differences in the structure of the epithelium of the maculas (less pronounced in that of the saccule), the height of the epithelium varying considerably in different areas. Fine canals exist between the supporting and the sensory cells for the terminal nerve fibers.

Opinions differ as to the exact structure of the cupula and its relation to the hair cells. Perhaps most observers agree that the cupula is composed of cylinders formed by the ramifying hairs, the cylinders being filled with a liquid. Stricht thought the cupula was composed of a system of cylinders, the walls of which were formed by the supporting cells and the centers by the protoplasm of the sensory cells. Opinions differ also with regard to the structure of the otolithic membrane. According to Quix, Kolmer and others, the otolithic membrane is attached to the macula by fibers coming from the supporting cells and by the short sensory hairs, which project like stakes into canals in the gelatinous mass of the otolith. Wittmaack's idea, which the investigations of Werner tend to support, is that the otolithic membrane is formed by a network of sensory threads, in the meshes of which the crystals of chalk are embedded. According to the latter observers, a delicate membrane separates the otolithic membrane and the sensory and supporting cells of the macula from the endolymphatic space. Other histologists deny the existence of this membrane. In the pike the otolith is suspended above the macula by a thick band arising from the marginal cells, the space between precludes the possibility of contact between the otolith and the macula. The vestibular nerve divides into two branches. The superior branch supplies the ampullae of the horizontal and the anterior vertical canals, the macula of the utricle and the upper part of the macula of the saccule. The inferior branch is distributed to the inferior part of the macula of the saccule, the ampulla of the posterior vertical canal and the cochlear nerve. A branch from the cochlear ganglion is said to go to the posterior part of the macula of the saccule. The terminal nerve fibers pierce the basilar membrane, losing their medullary sheaths, and form a calix, or plexus, around the sensory ciliated cells, penetrate between the sensory and supporting cells and end freely at the epithelial surface. They do not penetrate to the protoplasm of the cells. De No described large, medium and small nerve fibrils to the hair cells, which supply the central, lateral and marginal parts of the cristae, respectively. He distinguished also three regions of the macula of the utricle which have special types of termination of the nerve, the corresponding part of the otolith having a different structure. These differences are not distinguishable in the macula of the saccule.

Many investigations have been made of the position of the sensorial elements of the labyrinth in the skull. De Burlet has calculated mathematically the positions of the maculas and the semicircular canals. Quix measured the angles formed by the planes of the maculas with a plane of orientation (plane formed by the under surface of the occipital bone) and with the frontal, sagittal and horizontal planes, employing the skulls of various animals, including man. In man the angle formed by the anterior and posterior parts of the lapillus is 140 degrees, the angle between the anterior part of the lapillus and the horizontal plane is 59 degrees, the corresponding angle for the posterior part is 20 degrees, the lapillus forms with the sagittal plane an angle of 84 degrees. The two lapilli are at an angle of 167 degrees with each other. The angle formed by the two parts of the sagittae is 157 degrees, with the horizontal plane the anterior part forms an angle of 69 degrees, and the posterior part an angle of 82 degrees.

With the sagittal plane, the anterior part of the sagitta forms an angle of 46 degrees and the posterior part an angle of 22 degrees. The angle formed by the posterior parts of the two sagittae with each other is 44 degrees. With relation to the plane of orientation, the lapillus presents an angle directed forward, upward and outward, the sagitta presents an angle directed laterally, backward and upward. The planes of the utricular maculas lie almost horizontally. The saccular planes are situated symmetrically (but not in the same plane) in relation to the sagittal plane of the skull. The utricular macula forms with the macula of the saccule an angle of about 70 degrees. The planes of the semicircular canals of one side are at about right angles to each other. The planes of the two horizontal canals form an angle with each other of $173\frac{1}{2}$ degrees, their line of intersection forms an angle of 15 degrees with the basilar cranial plane. The planes of the two anterior vertical canals form an angle with each other of $82\frac{1}{2}$ degrees, and their line of intersection lies at an angle of 82 degrees with the basilar cranial plane. The angle formed by the planes of the two posterior vertical canals is 90 degrees, their line of intersection forms with the basilar cranial plane an angle of 88 degrees. In order to place the horizontal canals in a horizontal plane, the head must be inclined 30 degrees forward.

Static functions of the maculas of the saccules is denied by many writers. Werner has discovered anatomic particulars, both of form and of structure, in the utricle which indicate that this organ can exercise all the static functions. Histologic examination of the acoustic end organs is not without disadvantages. Both histologic preparations and direct observations are necessary for an exact determination of the structure.

DENNIS, San Diego, Calif

POSSIBILITIES OF VITAMIN C MANAGEMENT IN CASES OF INNER EAR DEAFNESS AND TINNITUS Z SZOLNOKY, *Monatschr f Ohrenh* **73** 707 (Nov) 1939

The author observed 50 cases of different cochlear disturbances. In the cases of chronic catarrh of the middle ear injections of vitamin C diminished the tinnitus, as they did in those of otosclerosis. In cases of arteriosclerosis of the inner ear—the majority of the cases observed—the improvement is due, the author believes, to the general increase of metabolism. Eight injections were given, two a week, besides a generally improved diet containing lemon. The results were marked improvement of hearing in more than half the cases and decrease of tinnitus and of blood pressure. In cases of acute neuritis also, this vitamin C shock, as the treatment is termed by the author, should be tried, as vitamin C seems to be an important factor for detoxicating the organism.

LEDERER, Chicago

ADENOMA OF THE CERUMINOUS GLANDS OF THE EAR W SPRENGER and F PRIETZEL, *Monatschr f Ohrenh* **73** 722 (Nov) 1939

A fibromatous tumor, which had originated from the superoanterior portion of the cartilaginous canal wall, near the tragus, was removed from the external ear canal of a 50 year old man. Histologically it appeared as glandular tissue of the nature of ceruminous glands and seemed to be benign. A few cases in which similar changes were noted are recorded.

LEDERER, Chicago

Pharynx

THE PLUMMER-VINSON SYNDROME DAVID P CORDRAY, *Ann Otol, Rhin & Laryng* **49** 160 (March) 1940

The Plummer-Vinson syndrome consists of anemia, glossitis and dysphagia. In addition, there is web formation across the opening of the esophagus. Differential diagnosis must embrace all forms of dysphagia at the upper end of the esophagus: ulceration from tuberculosis, syphilis or a malignant growth, stricture due to swallowing a corrosive, retropharyngeal diverticula, aneurysm, mediastinal tumors, cervical exostoses and, less often, central lesions resulting in bulbar palsy.

Experiments showed that secondary anemia in no way predisposes to the web formation, and it is thought that in the true Plummer-Vinson syndrome the web is the cause of the anemia, on account of its interference with nutrition. The experiments have caused the author to conclude that marked, protracted secondary anemia is capable of producing precancerous lesions in the esophagus, as the laboratory animals showed hyperkeratinization of the epithelial lining of the esophagus, with proliferation of the epithelial layer and an increase in the usual number of mitotic figures.

M V MILLER, Philadelphia

PUNCTURE WOUNDS OF THE MOUTH AND THROAT WOLFGANG KLIMPEL, *Ztschr f Hals-, Nasen- u Ohrenh* **45** 328, 1940

The author reports a group of 23 patients presenting puncture wounds of the mouth and throat, localized in the tonsil, soft palate, pharyngeal wall, anterior palatine arch and hard palate. These wounds are commonly made by children while at play and are produced either by their falling or by being struck while having a variety of substances in their mouths. The cases described include instances of injuries from glass tubes, metal tubes from toys, tin horns, wooden sticks and metal whistles. In adults the wound may be caused by a smoking pipe or some other foreign body.

In the cases reported, complications were rare. Treatment was usually conservative, with attention to drainage should infection occur. Removal of broken-off foreign bodies was also indicated. The author comments that the normal secretions of the mouth usually aided in rapid healing and, on the whole, did not encourage secondary infections.

PERSKY, Philadelphia

Larynx

THE SIGNIFICANCE OF HOARSENESS WALTER WELLS, *Ann Otol, Rhin & Laryng* **49** 99 (March) 1940

Hoarseness is a symptom in every case of some involvement of the larynx. It is often the only symptom present, even with an extremely serious laryngeal condition. The author discusses the conditions in which it chiefly occurs: voice strain, singer's node, pachydermia laryngis, acute and chronic catarrhal laryngitis, acute edematous laryngitis, acute spasmodic laryngitis (false croup), diphtheria (true croup), tuberculosis, syphilis, benign and malignant neoplasms and paralysis.

In a child who has hoarseness and difficult breathing unassociated with a cold and of long duration, laryngeal polyps should be suspected. These are the most common benign growths in children and may develop rapidly.

In persons in the neighborhood of 20 to 30, if there is persistent and recurrent hoarseness, especially if the patient is anemic and has a chronic cough, tuberculosis should be thought of.

Persistent hoarseness in patients above the age of 40 should suggest a malignant condition.

The mechanism of the larynx in causing hoarseness, the diagnosis of the various conditions and the treatment are briefly discussed. Emphasis is placed on removal of causative factors, vocal rest and proper instruction as to how to use the voice without strain when the acute symptoms are gone.

M V MILLER, Philadelphia.

THE VOICE AFTER LARYNGOFISSURE AND LARYNGECTOMY FOR CANCER OF THE LARYNX CHEVALIER L JACKSON, *Surg, Gynec & Obst* **70** 537 (Feb) 1940

The author has made an analysis of a questionnaire sent out to all his living patients operated on since 1929 for cancer of the larynx. Replies were received from 51 patients who had either one or both cords removed by laryngofissure and from 30 patients on whom a total laryngectomy had been performed. The questionnaire dealt primarily with the effects on voice.

In the group who had a laryngofissure, 43 have had a useful voice since the operation. Of the laryngectomized patients, 50 per cent replied that they have developed a fair voice.

In analyzing these reports, the author believes that the voice is of secondary consideration, since in the presence of a malignant tumor the life of the patient is at stake. However, his statistics show that the majority of the patients were able to develop useful voices and to resume their original occupations after either a laryngofissure or a laryngectomy. The majority of patients who developed a voice after laryngectomy considered it good, while the majority of patients who had a laryngofissure considered their voices only fair.

He advocates the employment of a systemic course of voice lessons to educate these patients in buccoesophageal speech. This training should be started as soon as the wound is healed, and, finally, an artificial larynx should not be tried until after the patient has made some effort to develop a voice without it.

PERSKY, Philadelphia

EXPERIMENTAL AND CLINICAL STUDIES OF PHARYNGEAL AND LARYNGEAL PARALYSIS. ARNE A. SJOBERG and EDWARD STROMWALL, *Ztschr f Hals-, Nasen- u Ohrenh* 45 322, 1940

While laryngeal paralysis is usually associated with a peripheral lesion involving the recurrent laryngeal nerve or the vagus nerve, either in the neck or in the mediastinum, a central lesion of the medulla, particularly in the region of the exit of the glossopharyngeal, vagus, accessory or hypoglossal nerves, may also produce a unilateral paralysis. This has been termed the hemibulbar paralysis syndrome.

The authors described the following lesions in this region: an intramedullary tumor, syringobulbia, disseminated sclerosis, acute bulbar paralysis, Wallenberg's syndrome with thrombosis of the posterior inferior cerebellar artery and a circumscribed syphilitic meningitis. Peripheral lesions may include a tumor of the base of the skull or in the epipharynx, tuberculosis, syphilis or fracture of the base of the skull in the region of the jugular foramen.

To establish a criterion for a more exact diagnosis, the authors have, through animal experimentation, attempted to isolate the independent actions of each of the four nerves in their relation to paralysis of deglutition and of the larynx. They cut the glossopharyngeal nerve in a group of 15 cats and observed the end results both by direct examination and by means of the endoscope.

A summary of their observations, both on these experimental animals and in clinical studies, is as follows: 1. In man, section of the glossopharyngeal nerve produces disturbance of taste and other sensory disturbances but no evidence of any interference of the motor functions of swallowing. 2. Recurrent neural paralysis with the midposition of the cords may be caused by lesions of the nucleus ambiguus or injury of the root fibers of the accessory nerve. 3. Section of the glossopharyngeal nerve in cats produces no paralysis of the pharynx, no lateral movement of the posterior pharyngeal wall (*mouvement de rideau* of Vernet) and no difficulty in the act of swallowing. 4. Section of the vagus nerve in cats produces a unilateral paralysis of the pharynx, *mouvement de rideau*, recurrent paralysis and the paramedian position of the cords. 5. Clinical and experimental studies have shown that the *mouvement de rideau* is due to a unilateral paralysis of the vagus and that the glossopharyngeal nerve has only a sensory function but no motor functions.

PERSKY, Philadelphia

Nose

MALIGNANCY OF THE NASAL ACCESSORY SINUSES WITH A REPORT OF TWO CASES OF PRIMARY CARCINOMA OF THE FRONTAL SINUSES. EARLE G. BREEDING, *Ann. Otol., Rhin. & Laryng* 49 141 (March) 1940

Primary carcinoma seems to be the most common variety of malignant growth at present. Carcinoma is most frequently seen during the fifth decade of life and

sarcoma chiefly in early life, the latter usually follows injury. The maxillary sinus is most frequently involved, the ethmoid, the sphenoid and the frontal come then in the order named. Involvement is usually secondary but may be primary. Chronic suppuration is probably the most frequent causative factor in carcinoma. There is usually some irritant present, such as chronic sinusitis, pressure from tumors or deformities or abscesses of dental origin.

The early growth is so insidious that there are no noticeable symptoms, later, swelling, pain, nasal discharge and frequently bleeding are seen. Headache, obstruction and foul discharge indicate advancement. Bleeding may be serious, because of erosion of the vessel. Anemia and loss of weight appear later. Usually only one side is involved. Biopsy and roentgen examination aid in diagnosis.

A malignant condition may be mistaken for sinusitis, a dentigerous cyst, a fibroma or an osteoma. It must be differentiated from tuberculosis, syphilis, foreign bodies and rhinoscleroma. In any patient over 40 nasal hemorrhage from one side recurring frequently, a prominence over the sinus, ulceration and fetid discharge, especially if the upper teeth are coming loose, should make one suspect the presence of a malignant growth. A hard, immobile growth, rapidly spreading to adjacent tissues and glands, in the presence of a negative Wassermann reaction, should be subjected to biopsy.

The prognosis depends on the type of neoplasm, its cellular structure, the age and general condition of the patient, the duration and the situation of the growth. The outcome is usually bad, but not so bad as formerly, as some cures have been reported, and life may be prolonged.

Treatment depends on the location, duration and type of growth. If surgical intervention is used it should be followed by roentgen and radium therapy and diathermic treatment.

The author reports 2 cases of primary carcinoma of the frontal sinus.

M. V. MILLER, Philadelphia

TWO CASES OF FIBROMA OF THE NASAL ACCESSORY SINUSES R. BALZER, *Ztschr f Hals-, Nasen- u. Ohrenh* 45 307, 1940

The author reports 2 cases of fibroma of the nasal accessory sinuses. In the first case a large tumor involved the ethmoid sinus, while in the second case the growth originated in the frontal sinus.

The particular interest in these cases is that histologic study of the tumor masses revealed typical fibromatous tumors with numerous areas undergoing calcification.

PERSKY, Philadelphia

Miscellaneous

DEEP NECK INFECTION AUGUST L. BECK, *Ann Otol, Rhin & Laryng* 48 940 (Dec) 1939

The author reports 78 cases of deep infection of the neck in patients varying in age from 8 months to 81 years. Over half the infections (53 per cent) involved the pharyngomaxillary space, 23 per cent were in the submaxillary space, 14 per cent were in the carotid sheath, 10 per cent were infections of the pretracheal fascia, 3 per cent were infections of the prevertebral fascia, and 21 per cent were suppuration of the cervical lymph nodes. *Streptococcus haemolyticus* appeared more often than any other organism, and some form of *Streptococcus* appeared in over 80 per cent of all infections.

As a rule unchecked infections of the neck end fatally through septicemia, asphyxia or hemorrhage, with proper care the great majority of patients recover. Recognition of sepsis is of utmost importance. Continuous high temperature, sometimes without visible swelling, may be expected from involvement of the lymphatics. High excursions of temperature with abrupt drops, with or without chills, may be expected from involvement of the veins. Frequently there are periods of drenching sweat. Spasm or splinting of muscles occurs when inflam-

mation involves them. Nerve involvement causes pain if sensory nerves are affected, paralysis, if motor nerves. As routes for lymphatic drainage are fairly well known, involvement of the various nodes may give a clue to the origin of the infection. Involvement of nodes adjacent to the vessels of the neck may lead to thrombosis and infection of the blood stream. If an abscess forms on a node it should be promptly drained.

Blood counts help in prognosis. A high white count with a moderate increase in polymorphonuclears is more desirable than the reverse. In the early stage of the infection, when it is severe, the eosinophils disappear, and with the lessening of the infection they reappear. The presence of more than 15 per cent of young forms of polymorphonuclears indicates that sepsis is becoming severe enough to cause irritation or disturbance in the bone marrow. When they reach 40 to 50 per cent an occasional myelocyte is expected, and the appearance of these is always of grave significance. A marked secondary anemia usually accompanies all severe deep infections of the neck.

The author discusses the various locations of involvement and the variable symptoms occurring with each. The complications which may appear, infections of the blood stream, phlebitis and thrombosis of the cervical vessels, edema of the larynx, empyema and mediastinitis, are all discussed. The analysis of his cases confirms previous conclusions that most frequently the cause of deep infections of the neck is primary involvement in or about the tonsils.

Early recognition of trouble is urged, and proper drainage should be instituted. If the patient is dyspneic because of edema of the larynx or a pathologic condition deeper in the respiratory tract, general anesthesia is contraindicated. Where it is due to pressure above the larynx a pharyngeal breathing tube makes general anesthesia safe. In the presence of dyspnea, narcotics should never be used. After tracheotomy a general anesthesia may be used safely provided the lungs are clear. Local anesthesia is used in deep infections of the neck only when conditions are present which make general anesthesia hazardous. If there is no inflammatory involvement of the parts good local anesthesia may be gained by reaching the cervical plexus at the posterior border of the sternomastoid muscle. If there is much inflammatory swelling it is difficult to anesthetize anything except the skin.

M. V. MILLER, Philadelphia

PLASTIC REPAIR OF GINGIVOBUCCAL ADHESIONS. CLAOUE, Oto-rhino-laryng internat **24** 41 (Feb.) 1940

The advantage of Claoue's method of repair of adhesions between the gums and the cheek is that recurrences are obviated. The technic is (1) an incision along the crest of the adhesion, (2) extension of the primary incision posteriorly along the gum and (3) an incision from the outer end of the first incision diagonally forward to the gum. This results in two triangular flaps with their bases toward the gum and the cheek respectively. After elevation and thinning of the flaps, the underlying scar tissue is removed. The anterior flap is slid inward along the incision in the membrane of the gum, the posterior flap is slid outward to approximate the outer edge of the anterior flap. It is important to dissect the buccal flap sufficiently to permit its being easily brought into apposition. Presumably the flaps are sutured.

DENNIS, San Diego, Calif

BEHAVIOR OF THE ORAL MUCOSA AFTER CUTANEOUS STIMULATION. C. CALABRESI, Arch ital di otol **51** 563 (Nov.) 1939

Calabresi studied the influence of cold applied to the skin of the extremities on the temperature of the tonsil and anterior pillar, using the thermoelectric couple of Benedict-Comel. Two groups of 15 subjects each, varying in age from 6 to 41 years, were investigated. The stimulus was applied by immersing the foot in a cold bath, kept at a constant temperature of 10 C. To the first group the stimulus was applied for twenty minutes, and temperature readings were made at two, five, ten, fifteen and twenty minute intervals from its application. To the

second group the stimulus was applied for five minutes, and readings were made at five and ten minute intervals after the stimulation. The results of the experiment were that in the first group the temperature of the oropharynx fell during the first five minutes and then rose to normal at the fifteen minute interval, to be again lowered between the fifteen and twenty minute period. In the second group, five minutes after the cessation of the stimulus the temperature of the oropharynx had risen rapidly to normal values, and at the ten minute interval the normal value was exceeded. Younger subjects showed greater reactions than adults.

DENNIS, San Diego, Calif

SEROLOGIC AND ALLERGIC REACTIONS OF SCLEROMA AND ITS SPECIFIC MANAGEMENT
E NEUBER, *Monatschr f Ohrenh* 2 58 (Feb) 1940

Through complement fixation and agglutination, the specificity of the bacillus of scleroma can be determined, and it can be differentiated from other encapsulated bacilli. With the aid of specific antigens, an allergic reaction can be achieved in the patient with scleroma. The best method is intracutaneous injection. Not only localized but also generalized symptoms appear which indicate that the vaccine might be successful. The allergic reaction evidences a reddened edematous halo after twenty-four hours, this is followed after a few days by a hard circumscribed infiltration, which remains for three to four weeks. The chemical and radiation methods of treatment have been discarded. The modern treatment is injection of specific vaccine. First, the general condition of the patient must be improved, a gold compound (aurothiodextrose, solganol B) has rendered best service in this respect. As an introductory treatment, small doses of this compound (0.01 to 0.25 Gm) up to 2 to 5 Gm total dosage are given. Then an autovaccine is used. The smallest amount of vaccine which still yields an allergic reaction is the initial dose, and the injection can be repeated in four to five days with slightly increasing doses. Constant watchfulness for local or generalized symptoms is required. Altogether, twelve to fifteen injections are given, and after six to eight weeks a second and if necessary a third combined gold and vaccine treatment is administered. The best results are achieved with the use of specific convalescent serum, four to six injections once a week in doses from 30 cc to 100 cc, intramuscularly. Blood transfusions from convalescent patients also give excellent results but are hampered by the fact that the blood groups have to be alike. In the author's opinion, the diagnosis and treatment of scleroma do not yield any more difficulties.

LEDERER, Chicago

PERCUSSION OF THE SKULL L BENEDEK, *Pract oto-rhino-laryng* 2 325 (Nov) 1939

The author constructed a rather ingenious apparatus for percussion of the skull, a mechanical hammer capable of giving a measured or regulated blow. In addition, he used an associated oscillogram which records the various sound waves. He attempted to differentiate the nature, the location and the dependence of the percussion note. He constructed an individual tone chart and tried to determine by the variations in the recordings on the oscillogram certain factors that would permit him to establish the nature and location of many intracranial lesions. Benedek states that he is able by this procedure both to differentiate and to localize abscesses of the brain, intracranial tumors and other lesions.

PERSKY, Philadelphia

SENSITIVITY, ANESTHESIA AND INNERVATION OF THE NASOPHARYNX A V GYERGYAY, *Acta oto-laryng* 27 519, 1939

Von Gyergyay has worked out the areas of the nasopharynx in which sensations of touch and pain are locally present and those in which pain is referred to the nose, the pharynx and the ear. He has also worked out the areas from which the gag reflex and the sneeze reflex arise. These areas are shown on

drawings The superior and posterior surface of the soft palate has little sensation nor is it capable of setting up reflexes In the velum the levator muscles have taken over the role of reflex excitors When the muscle is partially contracted the gag reflex is most pronounced If the muscle is fully contracted there is no gag reflex

For anesthesia of the nasopharynx he uses a thin 8 to 10 cm needle and injects the anesthetic into the outer third of each side of the soft palate one-half the distance between the attachment and the free edge Then, while the patient says "A" he injects further in a sagittal direction toward the side surface of the contracted levator muscles using 1 to 2 cm of a 1 to 2 per cent solution of procaine hydrochloride with epinephrine added After this he paints the upper choanal region of the nasopharynx with a mixture of cocaine and epinephrine

In making anatomic preparations of the region into which he makes the injection he has found, in addition to the well known pharyngeal plexus, which lies at the level of the oropharynx, a second smaller plexus lying higher up, which involved only the area of the nasopharynx and had connections with sympathetic fibers This network was connected with a ganglion lying in the upper outer point of the fossa of Rosenmuller He dissected branches going from this ganglion downward and inward and inward and toward the side wall His injection of anesthetic, therefore, involves the region of the motor nerve supply of the levator muscles and also the ganglion and nerve plexus just described

GROVE, Milwaukee

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